POSTGRADUATE MEDICINE

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See SAUNDERS Advertisement on pages 8 and 9

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OCTOBER 1951

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Leaves from a Doctor's Diary

By Maurice Chideckel

Sept. 1 . . . Right now I am endeavoring to master the anatomy of hate. Its thrust and power is devastating, its corrosive influence transcends the range of vision. In this our country, the land of freedom of conscience and freedom of worship, we have organizations whose members are counted in the hundreds of thousands—organizations which are formidable instruments for annihilation and for many of whose members cruelty becomes religious ecstasy. With furious energy, with destroying passion, they advocate discrimination, ostracism and persecution in the open or, like a restless undertow, preach detestation and animosity in the dark.

That atrocious vilification of innocent people who, by accident of birth, are either of a different faith or of a different color. No characterization fits those who sow dissension and envenom the minds of their listeners or readers. One cannot give a succinct description of them. Distortion of truth, misstatements, exaggeration and accusation of innocent people are their business. Their aim is to bring disaster upon the groups they hate. But what about those who are carried away by such knavery and treachery, most of whom are good Christian men and women?

I am wondering—is there an area of malignity in the cerebrum or cerebellum? Have the brains of these agitators been traumatized, causing destruction of tissue and depriving them of all things human? Did something occur in childhood that brought about a distortion of brain pathways? Or are there some mysterious unrevealed toxins in their brains that make them what they are? Is this hatred a form of toxic psychosis?

Some years ago one of those gentlemen died of malignancy for which the Jews were blamed. I was anxious to have a post mortem done. I was anxious to subject the brain and the ventricles to a microscopic examination. Maybe, I thought, I will discover some abnormality not found in the brain of normal men. The request was denied.

I ask, are those advocates of destruction to be condemned or pitied? Why do so many sensible people listen to those who preach hatred with resounding violence and flaming heat? Why is nothing being done to banish this scourge from our land? I searched the etiology in the principles of genetics and cytology as applied to man. I failed. In the dark little alleys of the mind there must dwell a demon that converts the human into a beast.

Can any profound analyst of human nature analyze the outrage of Cicero, Illinois? Why should there be cleavage between man and man? There is no answer to that.

After these thoughts I went outside for a bit of air and collided with eccentric Dr. Daniel. He said, "Hey, do you want to live long? Yes? Then don't waste a second of time. And do you know why the truth is valuable? Because you don't have to remember it. What? Why am I limping? Very tight shoes. Why don't I take them off?

You see, I have no enjoyment in life, not at all. My wife and I are separated, my children moved to faraway towns. I go to no movies, drink no liquor and play no cards. The only real pleasure I have in life is when I come home and take my shoes off. Oh, boy, what a wonderful, indescribable relief!"

* * *

Sept. 2 . . . Heard Mrs. Mooshe C. curse surgeon K. Said surgeon operated on her newborn grandson for duodenal obstruction of the intrinsic type. The infant died. The death was laid at the threshold of the doctor. The curse, as she folded her hands and gazed heavenward: "Oh Lord, ruler of the universe, grant that all the teeth of that butcher fall out with the exception of one, for toothache."

* * *

Sept. 3 . . . Many doubts have been sweepingly erased by the onrush of the progress of medicine. Modern scientific medicine symbolizes a stern fidelity to facts. Yet there are so many medical questions I cannot answer. Hypertension, for example. Is elevated blood pressure really a disease of adaptation, a manifestation of reaction to emotional stress, as stated by those who devoted themselves to the study of psychosomatic phases? Can one state with definite certainty that the causative factors of hypertension are actually rage, hostility, anger, jealousy and mental anguish?

The conviction or suspicion that her husband is unfaithful to her and that he is in love with another woman proved disastrous in the case of Clara Newell. She developed hypertensive encephalatrophy and paid with her life at the age of 31.

And there is Fanny Bergman, a fine physical specimen until a week ago. Today a hypertensive wreck. She had two boy friends, Sam and Louis. One night as she was vehemently kissed, she sighed romantically and said: "Again, Sam darling!" The lover sprang as if bitten by a venomous reptile and ran out, for it was Louis who had expressed his affection in vehement kisses. Worse, he sought out the other lover and told him. Now

(Continued on page A-20)

Anxiety and Autonomic Lability as the Basis of Functional Disorders

Emotional response to the stress of life is the primary source of illness in a steadily increasing number of cases. *Weiss* and *English*[1] estimate that as high as two-thirds of all patients have disorders due either entirely or in part to emotional factors and anxiety. *Ebaugh*[2] refers to anxiety as ". . . the universal disease of our times".

Complete examination discloses no organic basis for the symptoms in these cases, yet the clinical picture may mimic a true organic disease.

The symptom-complex usually involves several organ systems.[2,3,4] In such cases, the anxiety is channeled into organ dysfunction via the autonomic nervous system.[2,3,5,6] Some of the effects produced by exaggerated activity of a labile autonomic system are tabulated below. Many of these, it will be noted, are related to the symptoms which feature prominently in functional disorders. The symptoms in any one case are not necessarily limited to one organ system. Usually some are referable to sympathetic hypertonicity, others to parasympathetic hypertonicity.

ORGAN SYSTEM	SYMPATHETIC HYPER-TONICITY	PARASYM-PATHETIC HYPER-TONICITY	SYMPTOMS OF FUNCTIONAL DISORDER	AUTONOMIC LABILITY
GASTRO-INTESTINAL	Hypomotility Hyposecretion Intestinal Atony	Increased Salivation Hypermotility Hypersecretion	Belching Heartburn Nausea & vomiting Mucous diarrhea	When a patient exhibits a clinical picture suggestive of non-organic dysfunction, the diagnosis of Functional Disorder can be facilitated by use of the following indications of Autonomic Lability: Variable Blood Pressure Temperature Variations Changing Pulse Rate Deviations in B.M.R. Exaggerated Cold Pressure Reflex Oculo-cardiac Reflex Abnormalities Glucose Tolerance Alterations
CARDIO-VASCULAR	Rapid heart rate Peripheral vaso-constriction Slight rise in blood pressure	Reduced heart rate Vasodilatation Lowered blood pressure	Palpitation Sinus tachycardia Premature systoles B.P. low in some; elevated in others	
RESPIRATORY	Dry nasopharyngeal mucous membrane Bronchial relaxation	Increased nasopharyngeal secretion Bronchial constriction Laryngospasm	Dry mouth and throat Difficulty in breathing Sighing respiration	
GENITO-URINARY	Bladder detrusor relaxed; Sphincter contracted Ureter tone and motility decreased	Bladder detrusor contracted; Sphincter relaxed Ureter tone and motility increased	Urinary frequency Difficulty in urinating Dysmenorrhea Menstrual irregularity	

This tabulation is based on data available in references 1 to 6 stated below.

Primarily, the patient visits his physician out of concern over his symptoms. At this point, he is either unaware of his basic emotional problem or ignores it. A complete examination will rule out organic disease and thus reassure the patient. Then, treatment is directed along two lines: First, relieve the patient of subjective distress by drug therapy.* He will then be more cooperative in discussing his emotional problems. Then, having uncovered the basic problem, guidance is given toward correcting unhealthy situations and attitudes.

*The fact that autonomic dysfunction plays a large part in mediating the disturbance suggests autonomic sedation. A number of independent studies indicate that this therapeutic approach is effective.[7,8,9] The investigators used ergotamine tartrate (adrenergic blockade), levo-alkaloids of belladonna (cholinergic blockade) and phenobarbital (central sedation) in the form of **Bellergal** tablets. The total effect is an integrated sedation of the entire A.N.S.

1. WEISS, E., and ENGLISH, O.: Psychosomatic Medicine, ed. 2, Saunders Co., 1949. 2. EBAUGH, F. G.: Postgrad. Med. *4:* 208, 1948. 3. WILLIAMS, E. Y. et al: J. Nat. M. A. *42:* 32, 1950. 4. WOOLEY, L.: South. Med. & Surg. *102:* 157, 1940. 5. KATZ, L. N., et al: Ann. Int. Med. *27:* 261, 1947. 6. KROGER, W. S. et al: Am. J. Obst. & Gynec. *59:* 328, 1950. 7. KARNOSH, L. J., and ZUCKER, E. M.: A Handbook Of Psychiatry, Mosby Co., 1945. 8. HARRIS, L. J.: Canad. M. A. J. *58:* 251, 1948. 9. SLAGLE, G. W.: J. Michigan M. Soc. *41:* 119, 1942.

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she has lost both. "Oh, I thought that night was Wednesday, Sam's night. I forgot it was Tuesday, the night for Louis. And now—" She went into hysterical crying.

Here is Barbara Guilford, craving and dreaming of great wealth. Her rich old bachelor uncle bequeathed to her all his worldly possessions, including a mansion in California where an old flame of hers lives. The uncle, in his late 70's, was on his deathbed

with bilateral pneumonia and empyema. Barbara made all the necessary preparations to transmit him to eternity, and telephoned to her destined lover to spare no expense in rejuvenating their new home. Then dire calamity overtook her. The uncle recovered. Barbara, physically normal until then, entered my office with a 230/115 blood pressure. She suffered from severe headache, visual disturbances and giddiness. "He may live for 10 more years," she spoke weepingly.

Have these precipitations conflictual bases? Or are they merely coincidental?

* * *

Sept. 8 . . . Dietitian Collins, a learned unworldly man, sat in my office and discussed the ketogenic diet for the case of epilepsy he referred to me. "Ketogenic bodies are not yielded by carbohydrate. You get 90 per cent of the bodies in fat and 10 per cent in the carbohydrates. Now—" He suddenly interrupted himself. "I did not come for scientific discussions. It is altogether for another purpose. Don't you ridicule me, now, I am warning you. I am in love. Who is she? She is the woman who fulfills my concept of perfect femininity. She is the achievement of my dreams of the matchless, the sublime. She is coming to you for a physical examination. Please, I beg of you, be guarded in your speech. No jokes. She is too innocent, too sensitive."

She came. Face beautiful. Figure majestic. Her first words: "Hi, butch." She had already punctured my enthusiasm. "Jack Collins sent me here. He's nuts about me." Now her beauty was marred. Then: "Look here, I don't need no examination. You see, I got a touch of pregnancy. Now that goof must know nothing about it. Come on, shake a leg and fix it up for me. I've got to get married, see?" Now the salt had lost its savor. Nothing could be more repulsive, no countenance could look more forbidding than that of that morally crippled woman. I gleaned from her conversation that she had sampled a succession of lovers, and Collins was chosen as the winner. She looked angrily at me when I invited her out. Her last words: "I'll have to have an illegitimate bastard. Only over six weeks." Then she shook a finger at me. "Keep your trap shut tight if you know what's good for you."

* * *

Sept. 12 . . . What a wide gap there is between the thinking of one and that of another. Stolidity, stupidity and complacence I meet every hour in the day. Life's situations and emotions are poles apart from each other in each individual. Patricia Zerbini stealthily approached the parked car of her husband, found a woman in his arms and shot him dead.

Mrs. Pierce had left for her annual vacation and her husband, with the exhilarating conviction that his wife won't return for at least three weeks, decided it made life a gift worth having. I came to see the gentleman whose flexion deformity of the knee progressed to ankylosis of the joint. A little thing like chronic rheumatoid arthritis should not act as a barrier to the enjoyment of the charms of femininity. His beloved was there. The young woman, not bad to look at, was impatiently waiting for my departure. She may have had some more calls to make. As I neared the door she put her arms around him and began to do her work. In the hallway I collided with the "missus." She stood in the open doorway and watched the scene. The husband noticed her and let out a howl of pained surprise. It was the wife who was

embarrassed. Apologetically she explained her sudden return: "Sorry, I missed the train."

* * *

Sept. 15 . . . In the clinic.

Dr. W. too was interrupted just as he was demonstrating a tuberculous abscess for which the injection of penicillin was blamed. "This man," the nurse pointed to a big fellow, "is in great pain." From the doctor who speaks medicine only: "Ask him if the pain comes from the receptors of the skin or from the viscera." The patient: "From the rectum. The piles are killing me."

* * *

Sept. 21 . . . Sometimes facts are passed before me so rapidly that I cannot absorb them. One need not be unsparing in his delineation of faults and seams. Those faults, those unthinking cruelties, watching them, trying to analyze them, you just come to the conclusion that the human is still an unsolved mystery. Apropos this little incident.

Mrs. Hughes, 38, suffers from

(Continued on page A-22)

itching handle with care

When the itching infant urgently needs relief, his tender skin must be "handled with care" and therefore—no phenol (as in calamine $\overline{c}$ phenol), no cocaine, in fact no irritating or sensitizing agents. His loud and insistent appeal calls for

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1. Goodman, Herman: J.A.M.A. 129:707, 1945.
2. Lubowe, I. I.: New York State Journal of Medicine 50:1743, 1950.
3. Underwood, G. B., Gaul, L. E., Collins, E., and Mosby, M.: J.A.M.A. 130:249, 1946.

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bacterial endocarditis, chronic. Aureomycin and chloramphenicol did not do away with the infection. Yet, gasping for breath, she does her housework, collapses on the floor at times, rises and continues. Her husband, who professes deep love for his invalid wife, appears indifferent to her condition. Today he left for his vacation, leaving her alone in town. "She needs no vacation," he explained to me. "She doesn't work hard, certainly not half as hard as I do, and vacations cost money." I told him he may not find her when he returns. "Well, if the Lord so decrees—" and out he went.

* * *

Sept. 24 . . . In my waiting room.

J. J. suffers from abdominal bloating, evidently nongaseous. Said the wife: "Sweetheart, if the doctor says it's a cancer and you have to go soon, will you wait for me in Heaven?" The husband spoke up: "Didn't I always have to wait for you? But if I go, I am asking you, this time don't be long." Then the wife whispered in his ear: "Did you pay the premium?"

Mrs. Bugatch to Mrs. Jones: "I am unhappy. I am now convinced that my husband married me for my money." The kraurosis vulvae from which she suffers did not seem to concern her right now. And Mrs. Jones, on whom I just made a smear for acid-fast bacilli and found it positive, and who takes delight in hurting someone, answered: "Married you for your money. Well, congratulations. He is, after all, not as stupid as he looks."

David Day was away and his wife, whom he suspected of infatuation with his partner, Albert S., came to the office with that very partner. I know her to be a good virtuous woman who suffers from an inflammatory pelvic disease. Just as she was pouring out her heart to the aforesaid partner in came D. Day. The violent scene that followed was far from pleasant. The wife wept, David Day screamed and the partner laughed. "That fool," said he. "He knows I am impotent. What does he suspect me of?"

How quickly the month rolled away. Each month, the vanished four weeks appear to me a prelude to the Finale. That modicum of time called Life is, after all, but a brief flamboyant dream, ending in a terrified awakening. The short span consists of nothing but synonyms and antonyms, flat thuds and resonances, melodies and discords, straight lines and curvatures, flatness and convexness, sharpness and bluntness, these and nothing else.

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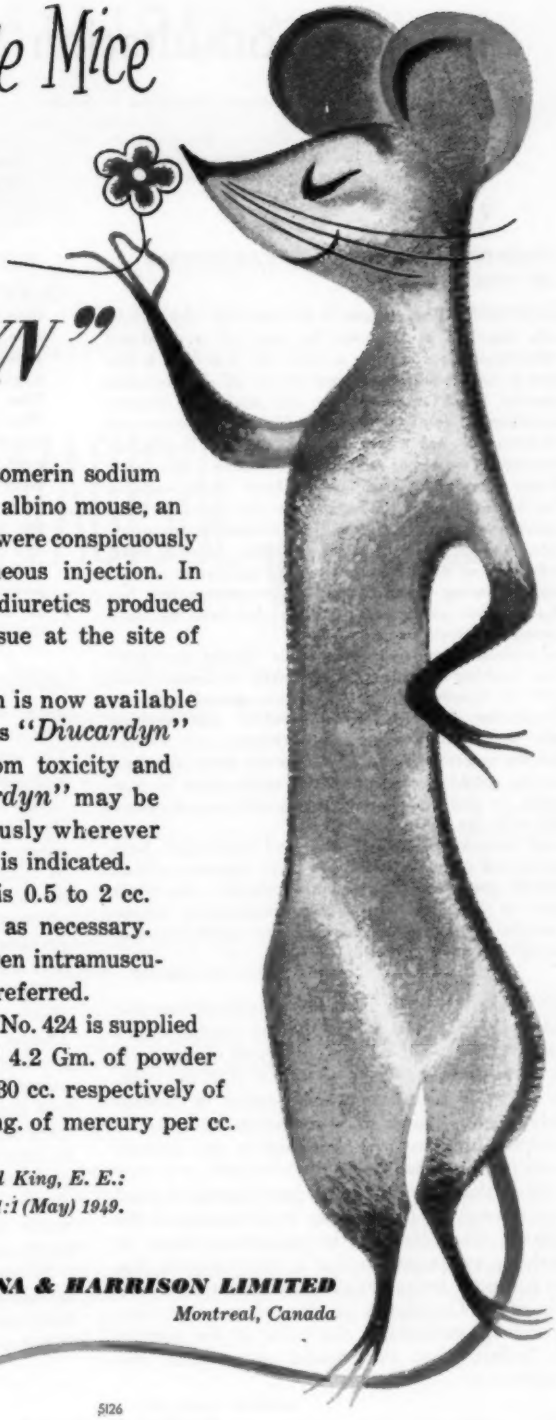

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**Lehman, R. A., Taube, H., and King, E. E.: Proc. Soc. Exper. Biol. & Med. 71:1 (May) 1949.*

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SYMPTOMS SUGGESTING CARCINOMA OF THE CARDIA

QUESTION: The patient, a 57 year old white woman, has had a diagnosis by x-ray of a duodenal diverticulum; for over a year she has had a low grade colitis with recurrent bouts of diarrhea-like stools. Stool examinations are negative, electrocardiogram is negative, white blood cell count and differential are normal. The patient is slightly anemic. Two weeks ago she had sudden emesis of a large blood clot and liquid blood while working in the mountains. Subsequently she fainted. Conservative treatment at the time helped her recuperate. A week later she had a sudden fainting spell while lying down; she recovered satisfactorily and since coming down from the mountains she has had a fairly good reaction. There has been no more emesis or blood in the stools.

The patient in general seems to be "going downhill" but nothing specific can be found to cause "colitis" or bloody emesis. A gastrointestinal series in December showed the diverticulum and nothing else except for a hypermobile cecum.

With the negative results of the recent gastrointestinal series, would a gastrointestinal malignancy be possible, or just what possibilities would sound plausible with the above history?

Blood pressure readings, pulse and respiration have remained normal, and chest x-ray appears normal.

I would appreciate any recommendation you might care to make as to probable diagnosis or recommended tests. She will have another gastrointestinal series as soon as plausible.

M.D.—California

ANSWER: A history of anemia, hematemesis and gradual deterioration of the physical condition of a patient 57 years old certainly suggests malignancy, and the hematemesis suggests that it is in the stomach. X-ray is notoriously unsuccessful in demonstrating early lesions of the cardiac end of the stomach. Gastroscopic examination is also unsatisfactory in this region.

I think that special x-ray technic should be used in an attempt to demonstrate a carcinoma of the cardia. If this fails and the patient continues to experience symptoms similar to the ones she has been having, I believe exploratory operation would be justified. Carcinoma of the cecum must also be carefully excluded as the cause of the anemia and "colitis," but this would not explain the hematemesis.

GEORGE CRILE, JR.

BLUISH DISCOLORATION OF THE GUMS

QUESTION: A single woman, aged 28, has a bluish discoloration of the gums of about five days' duration. She says the gums are tender but does not report any bleeding. The only other complaint is vaginal bleeding for a few days after menstruation. The physical examination gave negative results. The red blood cell count is 3,800,000, the white blood cell count 7500 and the hemoglobin 78 per cent. The differential count showed polymorphonuclear leukocytes 62 per cent, lymphocytes 27 per cent, eosinophils 8 per cent and monocytes 3 per cent. The red cells are normal in appearance and the coagulation and bleeding times are normal. Urinalysis is normal. There is no record of exposure to lead, mercury or bismuth or of the use of any unusual medication. What further study should be done for diagnosis?

M.D.—Illinois

ANSWER: Bluish discoloration of the gums may occur as a localized or a generalized disturbance. The causes may be either intrinsic or extrinsic. The most common extrinsic causes of generalized pigmentation are metallic intoxications in which bismuth and lead probably play the leading roles. On occasion, tobacco-chewing may discolor the gingivae, and localized blue areas may be caused by small imbedded pieces of amalgam. Pulmonary stenosis may also result in pigmentation. We have observed a bluish brown pigmentation following ATABRINE® intoxication and a similar pigmentation with Addison's disease.

The most likely cause in the particular case which you mention, however, is probably melanosis. This is usually mentioned as occurring as a racial peculiarity in dark-skinned persons and among the colored races. However, it has been my observation that this occurs in natural blondes and light races as well as among the darker pigmented individuals. The pigmentation of the gums often goes unnoticed for many years and the patient may discover it on self-examination and believe it is a recent change. I would suggest this as the most likely cause of the melanosis in this patient.

To complete your study, however, a biopsy may be made of the gingival tissue. If this is taken from one of the pigmented areas and the pigment is present it will be readily identified.

HAMILTON B. G. ROBINSON

(Continued on page A-40)

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When Doderlein bacilli and glycogen-laden epithelial cells are absent from the vagina, the pH may rise, and pus cells, Trichomonas vaginalis and pathogenic microorganisms usually appear.

On the basis of this and other findings of research, Vagisol has been formulated to produce a threefold result:

1) kill Trichomonas vaginalis, Monilia and certain pathogenic bacteria *on contact;*
2) restore vaginal glycogen;
3) re-establish Doberlein bacilli, which help to maintain *normal vaginal acidity.*

This it does without burning or irritating the vaginal mucosa, without stain or disagreeable odor.

Six ingredients give Vagisol swift effectiveness:

Phenyl Mercuric Acetate kills Trichomonas vaginalis and Monilia;[1,3] *Tyrothricin N. F.* works synergistically, increasing potency; *Succinic Acid* helps restore normal acidity;[3] *Papain* liquefies mucus;[4] *Beta Lactose* provides food for Doderlein bacilli, helps restore normal flora; *Sodium Lauryl Sulfate* reduces surface tension of secretions, increases penetration into vaginal folds.[5]

References

1. Johnson and Trussell: Chemotherapy of Trichomonas Vaginalis, Pro. Soc. Exper. Biol. and Med. 54, 245 (1943).
2. Henderson, John: Tyrothricin, J. A. Ph. A. 35, 151 (1946).
3. Fiorino, John F., Arrigoni, Louis, and Tozer, G.A.: An Improved Treatment for Trichomonas Vaginalis Vaginitis, Amer. J. of Obs., and Gyn. 59, 452-4 (1950).
4. Petermann, M. L.: Papain, J. Biol. Chem. 144, 607 (1942).
5. Emery and Edwards: Sodium Alkyl Sulfate, J. A. Ph. A. 29, 254 (1940).
6. Karnaky: Trichomoniasis, A Twelve Year Study, Western Journal of Surgery 54:61 (February 1946).
7. Boehme: Trichomonas Vaginalis, Vaginitis; Diagnosis, Treatment, Causes of Failure in Treatment, Surgical Clinic North America, pages 545-549 (June 1945).

SMITH-DORSEY DIVISION OF THE WANDER COMPANY
LINCOLN, NEBRASKA • Branches at DALLAS—MEMPHIS—LOS ANGELES

TREATMENT OF WEBER-CHRISTIAN SYNDROME

QUESTION: In the May 1951 issue of *Postgraduate Medicine* your consultant made the correct diagnosis as verified by biopsy of Weber-Christian syndrome in the case history submitted by me. Bacteriologic study of the specimen was negative.

Despite continuous administration of cortisone and salicylates with vitamin C, the patient continues to have recurrent bouts of fever associated with subcutaneous tender reddened nodules. The fever is usually brought under control by the temporary use of a supplementary dose of cortisone.

The following drugs have seemed totally ineffective: penicillin, aureomycin, terramycin, CHLOROMYCETIN®, GANTRISIN®, sulfanilamide, CHLOR-TRIMETON® and DICUMAROL®.

I would appreciate suggestions regarding therapy.

M.D.—Connecticut

ANSWER: There is no standard or consistently successful treatment for the Weber-Christian syndrome (relapsing nonsuppurative panniculitis) at present. One concept regarding the pathogenesis of this condition is that it is a type of hypersensitivity reaction which occurs locally in tissues as the result of varying primary causes.

In addition to the administration of cortisone and antibiotic agents, other methods of treatment which apparently have proved successful in some, but by no means all, cases, are:

1. Small doses of neoarsphenamine.

2. Intravenous injections of foreign protein, such as typhoid vaccine or PYROMEN®.

3. Filtered roentgen therapy to the involved areas.

In some cases, the disease is self-limited; in some, it responds to treatment, and in some the lesions have recurred in spite of all of the above-mentioned therapeutic measures.

EFFECT OF CORTISONE ON ABNORMAL CLOT FORMATION

QUESTION: I have a male patient aged 70, in vigorous health in most particulars except for arthritis of long standing in the knees. Following 30 injections of cortisone, an embolism with extensive adjacent edema developed in the right shoulder. This was treated surgically and healed promptly. Six weeks later a second embolism with mass edema developed in the right hip. This embolism has moved down to the upper calf muscles where a firmly congested spot may be felt, with tenderness over this spot and swelling of the entire calf and ankle. The hard spot seems feverish. There is no blanching of the feet or toes.

I wish to know if there is any evidence that cortisone can cause tendency to embolism.

What treatment can you suggest for a descending embolism in a leg. I would appreciate any suggestions.

M.D.—Tennessee

ANSWER: There is inconclusive evidence which suggests that cortisone may aggravate an already present tendency to abnormal clot formation. We have no experimental material to suggest that under normal circumstances the use of cortisone will initiate this tendency or, in itself, cause abnormal clot formation.

POSSIBLE KIDNEY DISEASE

QUESTION: An 18 year old boy has swelling of the face and ankles, possible fluid in the abdomen and some rales in the lungs. The heart seems normal. The blood pressure is 160 systolic, 110 diastolic. The specific gravity of the urine is 1010 and on testing the urine appears almost solid with albumin. There are no casts, blood or pus. The urea nitrogen is 20.2 mg., urea clearance 63 per cent, and the blood gives evidence of anemia with half the normal red cells and hemoglobin. I can find no source of infection. What is the possible diagnosis and what treatment should be followed?

M.D.—Montana

ANSWER: Much more information concerning the patient's history is necessary. What about childhood diseases? Other types of disease? How long have present symptoms existed? Has he ever been severely burned? Is he well developed physically and mentally?

I would make an intravenous urogram and take delayed films in two hours. The patient may have some congenital, developmental faults in the kidneys, ureters, etc. Has he large, dilated kidney pelves and ureters?

Treatment can be prescribed only after a complete diagnosis has been made.

GILBERT J. THOMAS

TREATMENT FOR IRREGULAR MENSTRUATION

QUESTION: A young woman, 21 years old, began menstruating when she was 13. Now she is extremely irregular. She may not menstruate for three or four months; then she will bleed for three or four weeks. My examination indicated excessive hair on the arms and legs and a male distribution of pubic hair. The patient is a school teacher. Would hormones be helpful?

M.D.—Missouri

ANSWER: From the history of this patient the suggestion is received of the regular shedding of the endometrium. I would suggest curettage and examination of the curettings by a competent pathologist. If within six months no improvement results a thorough examination for the lack of certain hormones might be helpful.

This is a difficult case and no good may come of it even after thorough examination and advice.

ROBERT D. MUSSEY

Therapeutic Indications for Vitamins in Mixtures

TOM D. SPIES, Birmingham, Alabama
ROBERT E. STONE,* Birmingham, Alabama
GUILLERMO GARCIA-LOPEZ, Havana, Cuba
RUBEN LOPEZ-TOCA, Havana, Cuba
ALFREDO REBOREDO,** Havana, Cuba

PRINCIPLES IN THE TREATMENT OF NUTRITIVE FAILURE

The story of clinical nutrition is one of brilliant deduction, careful observation and blind stupidity. The authors' concept of disease is that it is chemical in origin and chemically correctable. For 21 years this hypothesis has been the central motivating influence of our intensive and wide research in the field of human nutrition and metabolism. From the results obtained by our group and by other investigators certain practical applications gradually have accumulated. Perhaps the most difficult in application, but the most important from the standpoint of the doctor and his patient, is the concept of the use of vitamins in mixtures.

As a background we must understand that, to be well, the patient must eat properly. What he eats has much to do with his health and with his recovery from ill health. Optimal nutrition for every patient is a goal that the practicing physician should always keep in mind. (He must distinguish between what the community and even the family eats and what the individual, his patient, eats.) Many difficulties may confront the physician in getting the patient to follow a prescribed diet. Furthermore, the patient cannot always eat sufficient food to supply the nutrients in the amounts needed to correct his nutritional deficiencies, and often it is necessary to supply additional nutrients to supplement his diet. The many remedies recommended for the treatment of patients with nutritive failure may well be confusing to the practicing physician. Even those of us working in the field are not aware of all the preparations recommended from time to time, and many of these preparations vary greatly.

If we accept the statement, "We are what we eat," as a chemical truth, then how do these nutritional deficiency diseases occur? What happens when tissues become diseased? Does the process start gradually? Does an unbalanced chemical condition in our bodies initiate these changes? Does it promote the activity of the diseased cells? Is the cell, once diseased, capable

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*Clayton Foundation Fellow.

**Williams-Waterman Fellow.

Presented at the thirty-fifth (Chicago) annual Assembly of the Interstate Postgraduate Medical Association.

FIGURE 1

of healing itself? It is well to ponder these thoughts, but the physician cannot ponder long. He has the day-to-day problem of the medical management of nutritive failure and it is one of the most complex problems facing him today. Illustrative cases, we are told, are worth chapters of general description and discussion. Now down to cases.

Over 10 years ago a physician who is a friend of ours asked us to see the patient whose leg is shown in Plate I, not in consultation, for he had made a diagnosis of scurvy, but because we had had experience in taking colored photographs and he knew that this particular type of skin lesion was difficult to photograph. You will note the sharp areas of hemorrhage around the hair follicles. To the experienced physician these lesions often suggest the diagnosis of scurvy. After we had taken the photographs (Plate II), we asked our friend if we could make a few base line studies on the patient. This patient has been studied and treated by the physician and by our group on many occasions during the past 10 years. Since we had expressed an intense interest in the patient, the physician has gradually urged us to take complete responsibility, which we have done.

At the time the first photograph was taken, we found that the plasma ascorbic acid level was zero and, since she had false teeth, her gums showed no evidence of scurvy. This patient was given 500 mg. of synthetic ascorbic acid each day for three weeks. The lesions around the hair follicles faded within 72 hours and, as would be expected, the plasma ascorbic acid level increased.

At this time the patient's diet was evaluated. In Figure 2 it can be seen that she received a liberal amount of ascorbic acid (supplied therapeutically) but her intake of other nutrients was very inadequate. Miss Jean Grant, our head nutritionist, obtained samples of food from the patient's kitchen. We then divided a group of young white male rats into three groups. The diet of one group was restricted to the same diet as that of this patient. The second group received this basic diet plus some B vitamins and the third group received the basic diet plus liver extract.

All the rats looked similar when they were 51 days old and at the time the experimental evaluation of the diet was begun. The period of observation lasted until they were 100 days old. By the 100th day there was a great difference in the groups of rats, as can be seen in Figure 1. That there are still other nutrients essential for good nutrition is illustrated by the rat at the bottom of the figure. This rat received a supplement of liver extract and looks much healthier than the one which received only the supplement of vitamins. Those rats receiving the vitamins and basic diet looked better and were more active than those receiving only the basic diet.

From past observations on the effects of deficient diets on human beings, we were convinced that, since this patient lacked some of the essential nutrients in her diet, sooner or later she would develop symptoms of other deficiency diseases in addition to the scurvy which had been her presenting disease. Eventually this patient developed a macrocytic anemia. Later she was treated with folic acid for the first time.

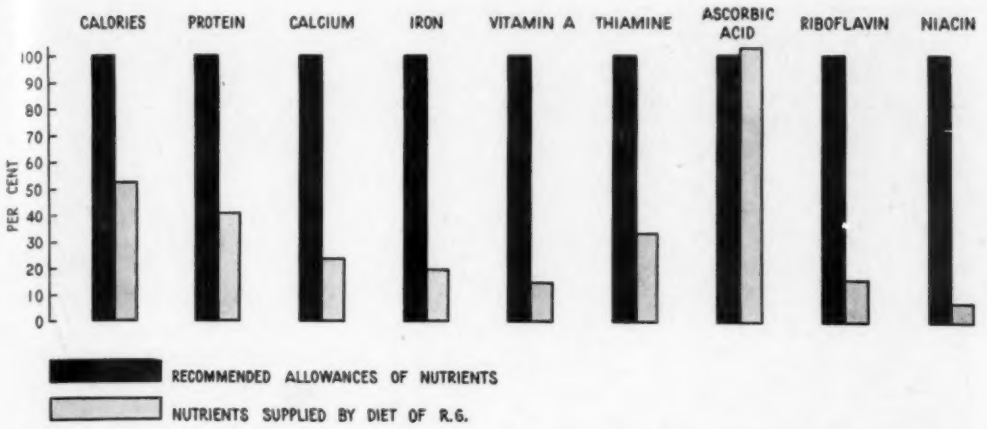

FIGURE 2. Nutrients supplied by diet of patient contrasted to allowances of nutrients recommended by the Council on Foods and Nutrition, National Research Council.

Folic acid often occurs in conjugated forms in nature and is present in yeast, liver and many other foods. It sometimes is referred to as pteroyl glutamic acid, its chemical name. From a therapeutic point of view, it should be kept in mind that either these conjugated forms of folic acid or the free form are effective in treating a folic acid deficiency.

Prior to the administration of folic acid to this woman, it was determined that she had a macrocytic anemia with a color index of above 1, megaloblastic arrest of the bone marrow and a histamine-fast achlorhydria. The findings of the gastrointestinal series were negative. No parasites or occult blood was evident in the stools. The striking improvement after the administration of folic acid can be seen in Plate III. Her tongue, which had been pale, was now very red. In many instances persons with normal-appearing tongues develop clinical glossitis temporarily after treatment, the reason being that glossitis is characterized by a fiery red color which in the absence of sufficient hemoglobin in the blood does not fully develop. Hence it becomes detectable upon later examination and sometimes after the patient has already improved somewhat. Eventually the glossitis was relieved completely by the parenteral administration of 15 micrograms of vitamin B_{12} every day for a week. We have found that a considerable number of patients who did not have anemia developed glossitis, which may be relieved by the administration of either folic acid or vitamin B_{12}, or both.

A few months after this woman had been treated with folic acid she developed pitting edema as can be seen in Figure 3. To determine its cause was a diagnostic problem. It occurred to us that it might be due in some peculiar way to anemia, to a protein deficiency which we knew to be present, or to some other factor as yet undetermined. She complained of easy fatigability, the sensation of heaviness and stiff-

FIGURE 3

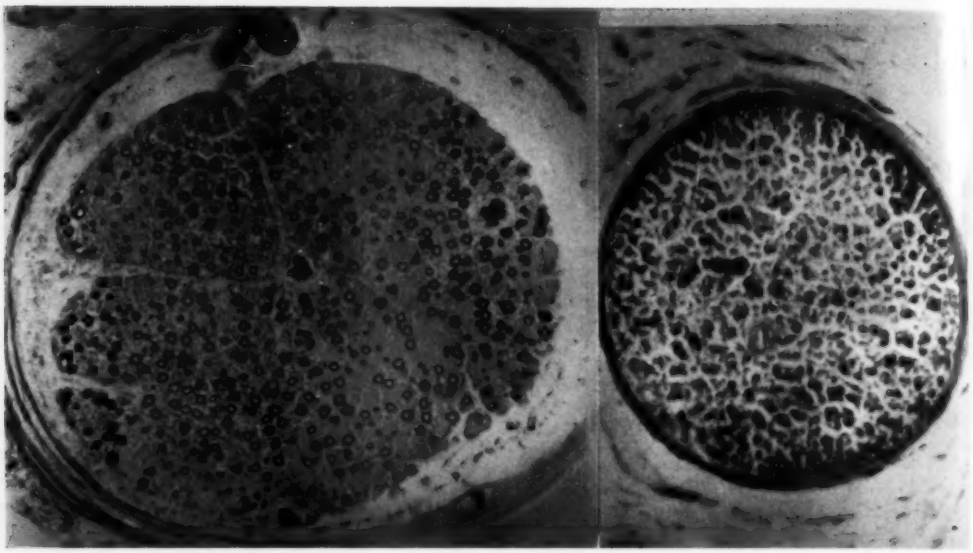

FIGURE 4

ness of the legs, and the inability to walk long distances. Soon after the development of these symptoms she noticed headaches, insomnia, nervousness and loss of appetite. When we examined her, we noticed that she had tenderness of both calf muscles. Realizing that she had had very little thiamine in her diet, we considered the diagnosis of beriberi, a disease rare in this country. Her blood chemical determinations were consistent with beriberi. A biopsy of a peripheral nerve taken from between her toes was made and a similar biopsy was made on a nerve of a control subject.

In Figure 4 on the left is the section of nerve from the control and on the right the section from the patient. Both were stained with osmic acid. Note the disappearance of the sheaths of Schwann, which is characteristic of vitamin B_1 deficiency and which supports the clinical impression of beriberi, in the nerve from the patient suspected of having beriberi. Fifty milligrams of vitamin B_1 in a sterile solution of physiologic sodium chloride was administered each day for a week. In 24 hours she had passed the amount of urine shown in Figure 5 and frequently she passed as much as a gallon of urine in 24 hours with the result that the edema soon subsided and she lost 31 pounds in body weight. Figure 6 shows this patient's legs after the clinical evidence of edema had disappeared. Note that they no longer look like the same legs as shown in Figure 3. According to the old terminology, it could be said that she had "wet beriberi" before treatment; whereas, after she lost the edema but still had some involvement of the nerve, it could be said that she had "dry beriberi." Acute symptoms, depending upon cardiac involvement, are spoken of as acute cardiac beriberi and the patient as having a "beriberi heart."

FIGURE 7 shows a patient who developed acute combined degeneration of the spinal cord. When we first saw this patient, she could not walk, had been bedridden for 48 hours and could not move any limb. A diagnosis of acute combined degeneration of the spinal cord associated with pernicious anemia was made. Fifty milligrams of thiamine was administered each day for a week. This did not help her in any way. After she had been given 30 micrograms of vitamin B_{12} intramuscularly each day for three days, she could stand as seen in Figure 7, could sit up and could comb her hair, all of which she previously had been unable to do.

A photomicrograph of vitamin B_{12} crystals is shown in Figure 8. As mentioned in an earlier paper,* vitamin B_{12} is the most potent chemical

*Spies, Tom D.: Recent progress in nutrition. Postgrad. Med. 6:96-106 (August) 1949.

FIGURE 5

substance per unit of weight which is used in therapy. An amount hardly visible is therapeutically effective. There is a whole family of the vitamin B_{12} substances. Vitamin B_{12a} and vitamin B_{12b} are identical. They were obtained by different investigators, one naming his substance vitamin B_{12a} and the other calling his vitamin B_{12b}. Vitamin B_{12} differs from vitamin B_{12a} (vitamin B_{12b}) in having a cyano group, which gives off CN when heated, as shown in Table 1. We will not discuss these substances in further detail except to say that there are other members of the family of vitamin B_{12} which are effective in such diseases as pernicious anemia, nutritional macrocytic anemia and sprue.

Figure 9 shows the response of a patient with pernicious anemia to a number of synthetic chemical substances. At different times—that is in each instance after an interval without treatment during which the patient ate her same diet and subsequently relapsed—she was given folic acid, 5-methyl uracil, vitamin B_{12}, vitamin

TABLE 1

1. Vitamin B_{12a} and vitamin B_{12b} are identical.
2. Vitamin B_{12} contains a cyano group which is not present in vitamin B_{12a}.
3. The cyano group is present in the vitamin B_{12} cobalt coordination complex.
4. Cobalamin designates all the vitamin B_{12} molecules except the cyano group. Vitamin B_{12} can then be termed cyano-cobalamin and vitamin B_{12a} termed hydroxo-cobalamin.
5. Both have been found active by parenteral injection in producing clinical and hemopoietic improvement in persons with pernicious anemia, nutritional macrocytic anemia and tropical sprue.

B_{12a}, vitamin B_{12b}, and folinic acid (sometimes called the citrovorum factor). As can be seen in Figure 9, there was an increase in reticulocytes and a hemopoietic response following the administration of each of these substances. We will not elaborate upon the various substances capable of producing blood regeneration. Our thought as to why there are so many substances is that, in order for you and us to be able to make blood, nature does not rely upon just one chemical molecule but furnishes a number of molecules, each of which will initiate blood regeneration.

The typical dermatitis of the dorsa of both

FIGURE 6

FIGURE 7

hands of a patient with pellagra is shown in Plate IV. This picture was made a number of years ago, for pellagra has now been virtually eradicated in the South, although in the North there are still cases of it to be found.

Had she not become pregnant, perhaps this patient would not have developed clinical evidence of pellagra, since it is not uncommon for the first detectable symptoms of pellagra to be seen during pregnancy. Two years later this 26 year old woman, mother of a 6 month old nursing infant and two other children, 6 and 8 years of age, was admitted to the hospital complaining of weakness, diarrhea and a sore red tongue. The nursing infant was admitted with her.

She gave a history of weakness and failure to "pick up" for three or four months after the birth of each of the two oldest children who were breast-fed. After the birth of the third child she "never did pick up—just kept going downhill." Throughout each pregnancy her appetite had been poor and her diet had consisted chiefly of small amounts of the foods she liked best—rice, potatoes, bread, fruit and desserts. She rarely ate eggs, meat or fish, ate vegetables only occasionally and drank only about three glasses of milk a week. Diarrhea and soreness of the tongue, which had been intermittent since a month before the birth of the child, became almost constant two weeks before she was admitted. Within a few days she was so weak she was forced to stay in bed.

Physical examination of the mother showed a pale, weak, thin woman with moderately severe glossitis. Laboratory studies showed a flat glucose tolerance curve, the presence of free hydrochloric acid in the gastric juice, and watery, brown-colored stools. Peripheral blood findings of severe macrocytic anemia were found. The bone marrow showed typical megaloblastic arrest. A diagnosis of macrocytic anemia of pregnancy was made. Physical examination and laboratory studies of the nursing infant showed her to be normal and healthy.

On a previous admission, the mother was given 10 mg. of folic acid daily by mouth. The reticulocytes increased to 37 per cent on the seventh day of therapy. The glossitis began to fade and her tongue was less sore on the third day of therapy, and by the fifth it was normal in color and the soreness had disappeared. The

FIGURE 8

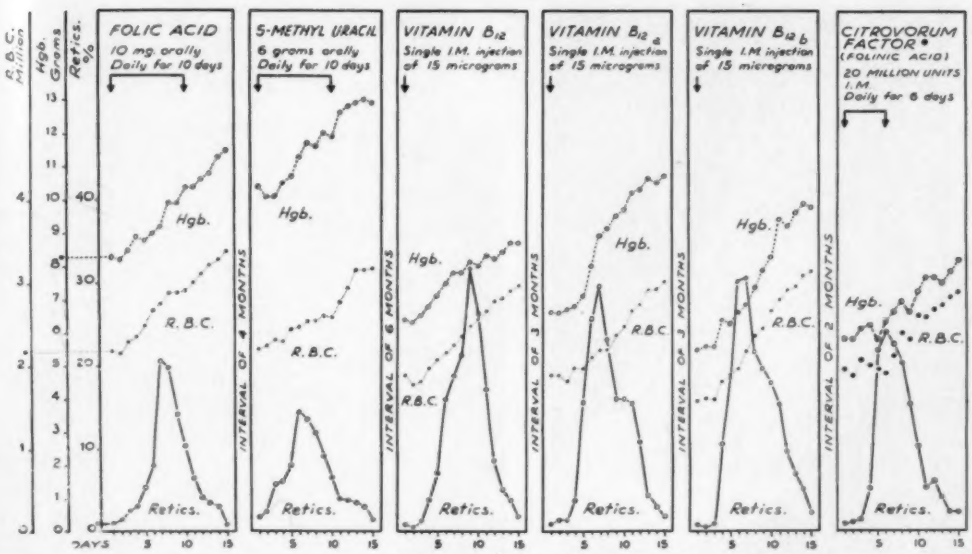

FIGURE 9. Hemopoietic response of a patient with pernicious anemia to folic acid, to 5-methyl uracil, to vitamin B_{12}, to vitamin B_{12a}, to vitamin B_{12b} and to citrovorum factor (folinic acid).

*1 unit of citrovorum factor is equivalent to 0.0001 microgram of pteroyl glutamic acid (folic acid); in other words 10 million units equal 1 mg. of pteroyl glutamic acid.

diarrhea began to subside on the fifth day and by the tenth day the stools were normal. On the twentieth day of folic acid therapy she asked to be allowed to go home because her husband was ill. By this time her blood values were: red blood cells, 4.02 million; hemoglobin, 11.3 gm. (78 per cent); reticulocytes, 1.0 per cent. She was given instructions in regard to the food she should eat, discharged from the hospital and asked to return every two weeks for follow-up studies.

We did not see the patient again until two years later when she brought her fourth child, a 9 month old nursing female infant, to us for treatment. At this time she said that she had not returned previously because she had moved too far away from the hospital. She said that she had been well until six months before the birth of this child when she lost her appetite, developed intermittent diarrhea and rapidly lost strength. Until she lost her appetite she had followed the diet recommended at the time she was discharged from the hospital two years previously; then, she began eating only small amounts of bread, rice, desserts, soups, fruit juices and milk. Four weeks following the birth of the child her appetite returned, she ate a more adequate diet and slowly her health improved. Study of the peripheral blood showed her blood levels to be within normal range.

The mother said that the infant seemed normal and healthy at birth when she was started on breast milk feedings and that she had had no other food of any kind since. When the child was four months of age she began to cry a great deal and her parents noticed that she was unusually pale. Up until this time the child had been constipated but she then began having occasional bouts of diarrhea consisting of several brown, watery stools daily. Her pallor increased, she lost weight, began refusing most of the breast milk feedings and slept most of the time. When she was awake, she cried almost constantly. The mother said the child felt "dead" when she picked her up and the neighbors told her the child could not live.

Physical examination showed a small, underweight child who appeared to be considerably younger than 9 months of age. The skin had a waxy pallor. The muscles were soft and "doughy" to touch. She lay quietly in bed with her eyes closed and, when aroused, whimpered, then fell asleep again. She could not hold up her head without support and appeared more helpless than a newborn infant.

PLATE I

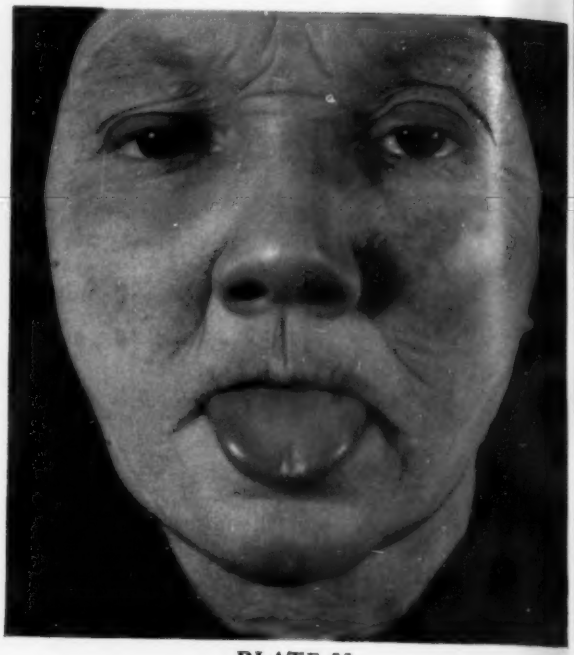

PLATE II

PLATE III

PLATE IV

PLATE V

PLATE VI

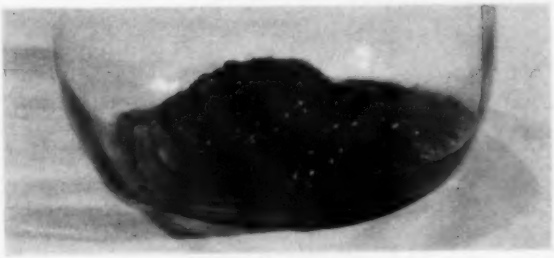

PLATE VII

PLATE IX

PLATE VIII

The blood values on admission were: red blood cells, 1.11 million; hemoglobin, 4.2 gm. (27 per cent); reticulocytes, 1.0 per cent.

She was given 10 mg. of folic acid orally daily for four days. On the second day of therapy the reticulocytes began to increase and four days later they reached a peak of 25.6 per cent. The red blood cells and hemoglobin increased rapidly. Two weeks after folic acid therapy was started the blood values were: red blood cells, 3.11 million; hemoglobin, 9.3 gm. (60 per cent); reticulocytes, 5.1 per cent. (See Figure 11.)

On the second day of therapy there was a striking improvement in the child's appearance; she was smiling and sitting up in her mother's arms. When a sample of blood was taken from her finger she cried, whereas prior to therapy she lay with her eyes closed and apparently did not feel her finger pricked. The mother said that she had taken all her breast milk feedings so far that morning and cried for more. By the third day of therapy her skin had a pinkish cast. After the fourth day of therapy the diarrhea disappeared and did not recur and the stools appeared normal. Clinical improvement was rapid. Two weeks after therapy was initiated she was as active as a normal healthy child and her color appeared normal.

Twenty days after folic acid was discontinued the red blood cells had decreased to 2.57 million and the hemoglobin to 7.0 gm. (45 per cent) but clinically the child appeared well. It was decided to give her a single 10 microgram intramuscular injection of vitamin B_{12}. Five days later the reticulocytes peaked at 28 per cent. A prompt increase in red blood cells and hemoglobin followed. By the eighteenth day after the injection of vitamin B_{12} the red blood cells had increased to 4.40 million and the hemoglobin to 11.9 gm. (77 per cent). (See Figure 11.) Eighteen months after she was given antianemic therapy, the child appeared well and there had been no recurrence of diarrhea. The red blood cell count was 4.71 million but the hemoglobin had decreased to 8.7 gm. (56 per cent), which probably was due to a deficiency of iron in her diet. Accordingly, she was given 0.3 gm. t.i.d. of solution of ferrous sulfate.

FIGURE 10 shows clearly that the macrocytic anemia of pregnancy does not respond to vitamin B_{12} when injected or when given orally, but it does respond when folic acid is included in adequate amounts. Vitamin B_{12} does not promote blood regeneration in a patient with the macrocytic anemia of pregnancy, whereas folic acid does. Accordingly, it can be stated that folic acid and vitamin B_{12} both have their special function, although their usefulness appears to overlap. Never forget that they both are essential vitamins. Never think that one can be substituted for the other.

A Cuban patient is shown in Plate V. His diet was similar to that of the woman shown in Plate IV—similar in that it was low in calories, low in proteins and relatively high in refined fats and carbohydrates, but it differed in that some of the vegetables eaten in Cuba are not eaten in the United States. A diagnosis of typi-

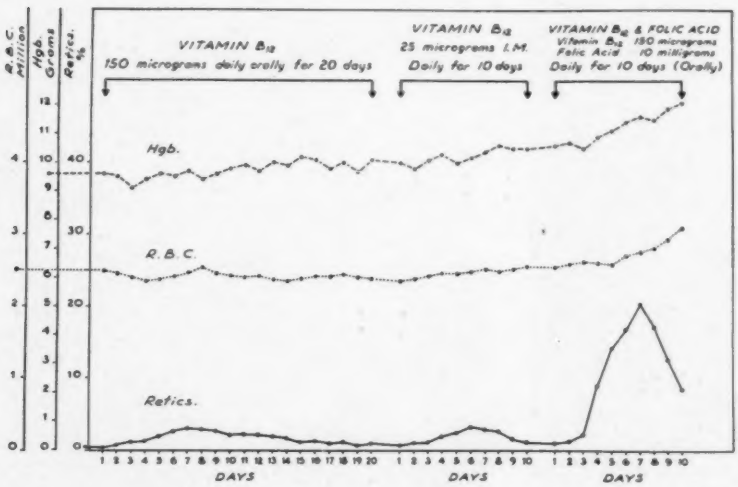

FIGURE 10. Failure of hemopoietic response to vitamin B_{12} administered orally and intramuscularly contrasted to response to the oral administration of a combination of vitamin B_{12} and folic acid in a patient who has macrocytic anemia of pregnancy.

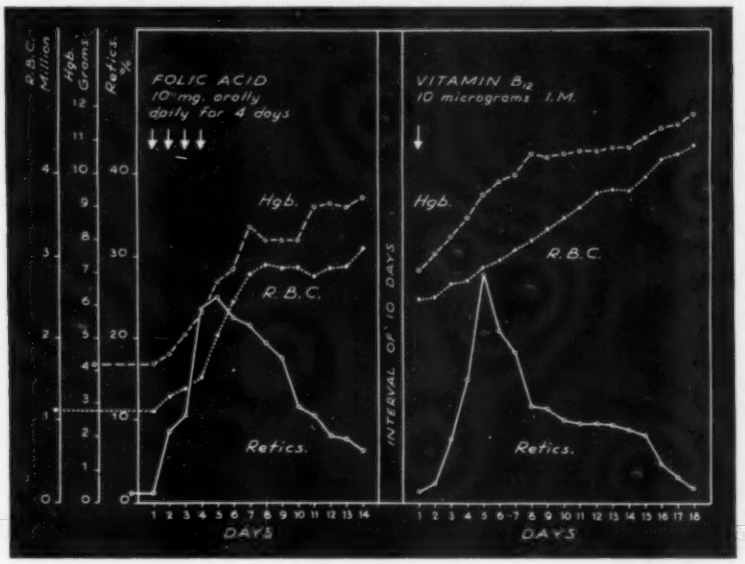

FIGURE 11. Hemopoietic response of a 9 month old infant with megaloblastic anemia of infancy to folic acid and to vitamin B_{12}.

cal tropical sprue was made. The smears from the bone marrow puncture (evident in the illustration) showed that he had typical megaloblastic arrest of the bone marrow. He had a characteristic red tongue, his skin had a lemon yellow tint and he appeared to be extremely undernourished. Plate VI shows a stool a few hours after it had been passed. From the bubbles of gas it is evident that a great deal of fermentation already had occurred. After three days of treatment with folic acid, there was a great change in the stool (Plate VII). Note the decrease in volume and the appearance of normal pigments in the stool. (Bowel movements were no longer accompanied by pain.) Four days later his stools appeared normal.

The macrocytic anemia of this man is typical of severe sprue in relapse. Many different chemical substances (nutrients) were used in the treatment of this case of sprue, and each produced blood regeneration (Figure 12). Either vitamin B_{12} or folic acid tends to relieve the patient of the diarrhea associated with sprue. In occasional cases, one is effective while the other is not. Sometimes, but rarely, it appears that when folic acid and vitamin B_{12} are administered together, they are more efficacious in inducing a normal return of alimentary tract function than when either is administered separately.

When acute or subacute degeneration of the spinal cord develops in persons with pernicious anemia, it is necessary to treat this condition either with vitamin B_{12}, one of the members of the vitamin B_{12} family, or substances containing them, since folic acid therapy neither relieves nor prevents nerve degeneration (Figure 13). As can be seen, folic acid therapy produced a satisfactory blood regeneration but the patient developed acute degeneration of the spinal cord. Following the administration of vitamin B_{12}, the symptoms arising from degeneration of the spinal cord disappeared. If the symptoms are acute in onset, they tend to disappear rapidly after treatment, but if the condition is chronic the changes often are irreversible. In such cases vitamin B_{12} will not relieve the symptoms completely and in some instances may give little or no relief.

The amount of weight gained while the patient was on folic acid therapy is shown in Figure 14. This occurred despite the usually poor

TABLE 2

"FOLIC ACID" CONTENT OF FOODS

HIGH	MEDIUM	LOW
Fresh dark green leafy vegetables	Beef	Root vegetables
Liver	Veal	Tomatoes, bananas
Cauliflower	Dry wheat breakfast cereals	Milk, cheese
Kidney		Pork, ham, lamb
		Rice, corn meal, sweet potato

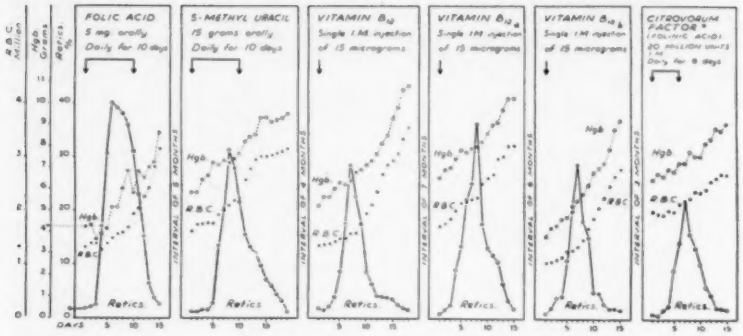

FIGURE 12. Hemopoietic response of a patient with pernicious anemia to folic acid, to 5-methyl uracil, to vitamin B_{12}, to vitamin B_{12a}, to vitamin B_{12b} and to citrovorum factor (folinic acid).

*1 unit of citrovorum factor is equivalent to 0.0001 microgram of pteroyl glutamic acid (folic acid), in other words 10 million units equal 1 mg. of pteroyl glutamic acid.

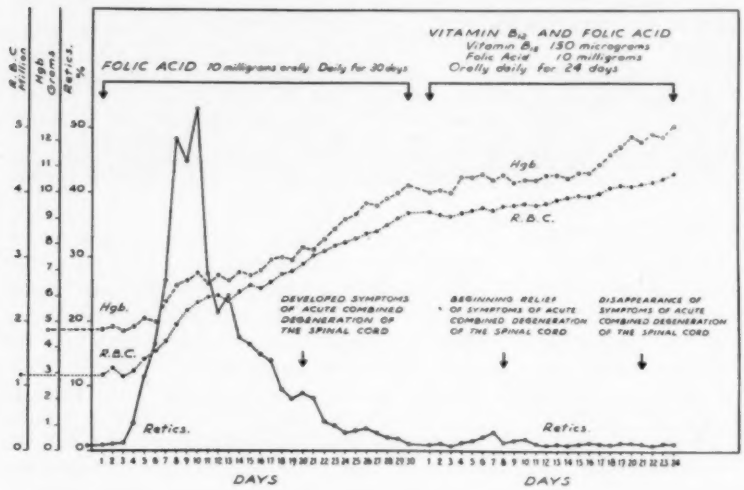

FIGURE 13. Hemopoietic response and development of acute combined degeneration of the spinal cord in a patient with pernicious anemia: disappearance of acute combined degeneration of the spinal cord on folic acid and vitamin B_{12} therapy.

diet of the patient; however, it does not mean that folic acid, per se, produced the gain in weight, but that it stimulated the patient to eat so much more that his caloric intake was increased. When discharged from the hospital, he was able to go to work and earn enough money to buy proper food. Taking into consideration the folic acid content of foods, we advised him as to what foods he should eat in order to remain well (Table 2).

Plate VIII shows one of the two children in a family we have been studying. Frequently all the members of families do not eat the same foods, with the result that different nutritional deficiencies may appear in different members of the family or one member may have clinical evidence of one or more nutritional deficiencies while other members may have no evidence of such deficiencies. This child has riboflavin deficiency as evidenced by the presence of cheilosis.

A child with rickets is shown in Plate IX. Previously I remarked that the North had not rid itself of pellagra; I wish to mention here that the South has not eradicated rickets. Rickets nearly always occurred in Negroes, chiefly because they did not have enough sunlight exposure. The great majority of Negro children, however, do not have clinical evidence of rickets.

Figure 15 illustrates the multiple deficiencies of nutrients in the diets of families with nutritional deficiency diseases. A study of this illustration shows that it is not reasonable to expect only one nutritional deficiency disease to be present. Every so often I am asked what guide should be used in order to have good nutrition; a satisfactory answer is given in Table 3. Nutritive failure can be relieved by applying the principles of therapy illustrated in Table 4. In

TABLE 3

A GUIDE TO GOOD EATING

Milk	2 or more glasses a day for adults 3 to 4 or more glasses daily for children (to drink and combined with other foods)
Vegetables	2 or more servings daily besides potato (1 raw; green and yellow often)
Fruits	2 or more servings daily (1 citrus fruit or tomato)
Eggs	3 to 5 a week; 1 daily preferred
Meat, Cheese, Fish or Legumes	1 or more servings daily
Cereal or Bread	Most of it whole grain or "enriched"
Butter	2 or more tablespoons daily
Other Foods to Satisfy Appetite and Complete Growth and Activity Needs	

TABLE 4

FOUR ESSENTIALS FOR THERAPY IN NUTRITIVE FAILURE

1. *Diet*	4000 calories, 120 to 150 gm. protein, rich in vitamins and minerals
2. *Basic Therapy*	thiamine, riboflavin, niacinamide, ascorbic acid, folic acid orally and vitamin B_{12} when it can be absorbed
3. *Additional Medication*	synthetic vitamins as indicated, orally or parenterally
4. *Natural B Complex*	brewers' yeast or extract and/or liver extract orally or parenterally

making this recommendation I am taking for granted that the persons having nutritive failure are underweight. If they are obese, of course, it is unwise to give them 4000 calories; however, one should keep in mind that obese persons can have vitamin deficiencies too.

As far as I know, there are two injectable preparations containing many of the water-soluble vitamins: SOLU-ZYME® and FOLBESYN®. The hemopoietic response of a patient with nutritional macrocytic anemia to the former is shown in Figure 16 and to the latter in Figure 17. I am not partial to either of these preparations. It is difficult to obtain cases which are identical, and it is not significant that the reticulocyte response is higher in one case than the other.

It is well to keep in mind that ascorbic acid has a deleterious effect on vitamin B_{12}. These two substances cannot be in contact for too long a period of time without the inactivation of vitamin B_{12}. They can be mixed without difficulty, however, just prior to injection.

Table 5 shows a basic summary for treatment with synthetic vitamins. The reason for using the words "and activator" with vitamin B_{12} is to remind the physician that such a thing en-

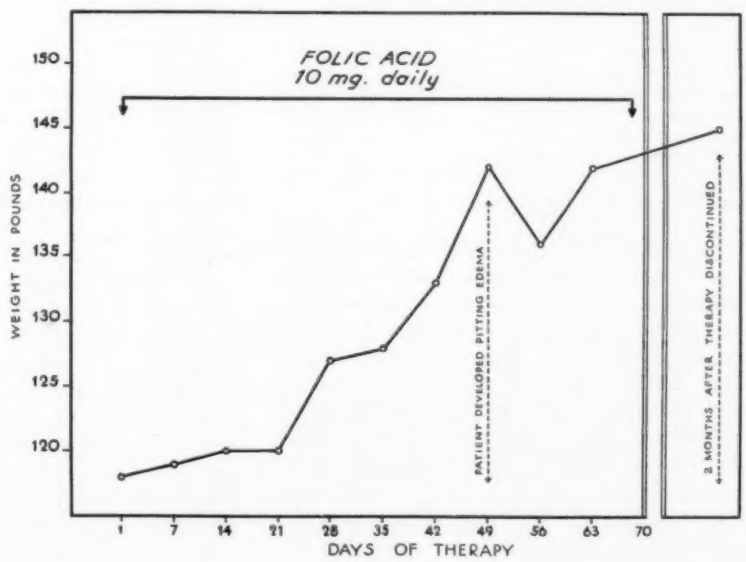

FIGURE 14. Weight gain of patient with sprue.

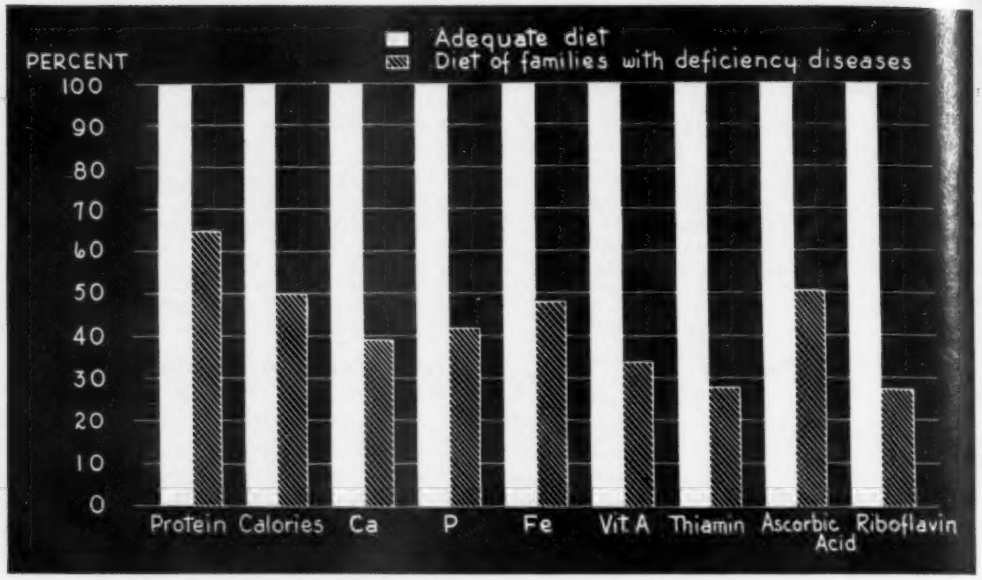

FIGURE 15. Average dietaries of families with deficiency diseases compared with an adequate diet.

The degree of nicotinic acid deficiency in the dietaries cannot be evaluated from the data on the nicotinic acid content of food available at the present time.

The majority of persons in these 20 families had clinical symptoms of pellagra, beriberi, scurvy, riboflavin deficiency or vitamin A deficiency.

TABLE 5

BASIC FORMULA FOR TREATMENT WITH SYNTHETIC VITAMINS

In treating the clinical syndromes of sprue, beriberi, pellagra, riboflavin deficiency, scurvy and certain macrocytic anemias the following basic formula is used:

	DAILY
Folic acid	5 mg.
Thiamine	10 mg.
Niacinamide	150 mg.
Riboflavin	10 mg.
Ascorbic acid	150 mg.
*Vitamin B_{12} and "activator"	10 mcg.

*Equivalent to 10 micrograms of vitamin B_{12} and intrinsic factor adequate to form its conjugate.

ables a patient taking vitamin B_{12} by mouth to absorb more of this vitamin, but there is no satisfactory preparation of it on the market at the present time. We recommend parenteral therapy for patients with pernicious anemia, since some of them cannot absorb vitamin B_{12} through the gut wall. In past years these pernicious anemia patients died, although there was vitamin B_{12} in their intestines. Nevertheless, it is interesting that many patients can absorb vitamin B_{12} by mouth rather well.

Very recently 3000 micrograms of vitamin B_{12} crystals* were given in a single oral dose to each of 3 patients with pernicious anemia and 2 patients with tropical sprue in relapse. A prompt reticulocyte response and an increase in red blood cells and hemoglobin occurred. The general clinical conditions of the patients also improved. None of these cases reached a theoretical maximal response, yet all of them did respond. In each instance a definite response began on the second day following therapy. The glossitis and stomatitis promptly healed and had disappeared by the fourth day. These observations show that a rather small amount of vitamin B_{12} is absorbed from the alimentary tract of patients with either pernicious anemia or tropical sprue.

As shown in Figures 9 and 12, the parenteral injections of the citrovorum factor (folinic acid) to persons with certain types of macrocytic anemia in relapse result in a reticulocytosis followed by a subsequent increase of the red blood cells and amount of hemoglobin. This hemopoietic response is associated with clinical improvement. In no patient with anemia have we found that the citrovorum factor does anything that folic acid does not do. (That is, we have

*Furnished by Dr. Stanton Hardy, Lederle Laboratories.

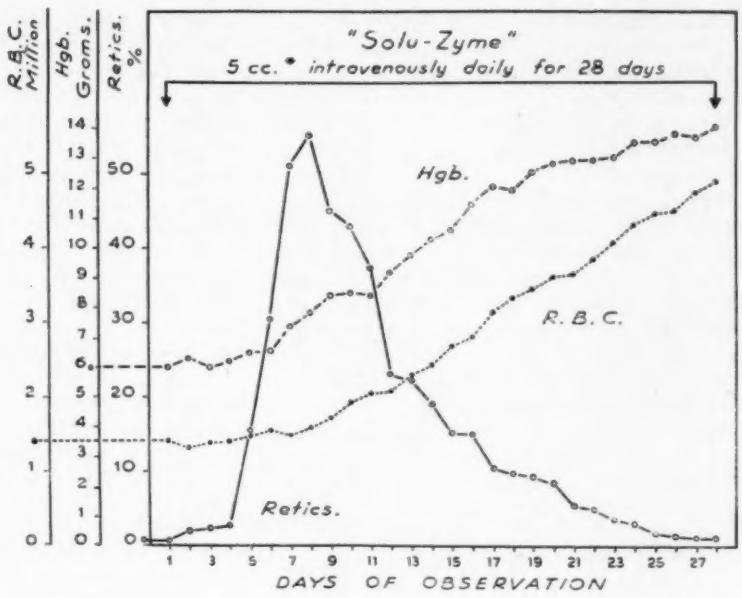

FIGURE 16. Hemopoietic response of a patient with nutritional macrocytic anemia to SOLU-ZYME®.

*Each 5 cc. contains:

Vitamin B_{12}	5 mcg.
Folic acid	5 mg.
Riboflavin	10 mg.
Niacinamide	250 mg.
Thiamine hydrochloride	10 mg.
Pyridoxine hydrochloride	5 mg.
Sodium pantothenate	50 mg.

Supplied as a sterile dry powder with a separate 5 cc. vial of fluid containing 500 mg. ascorbic acid for preparing the solution.

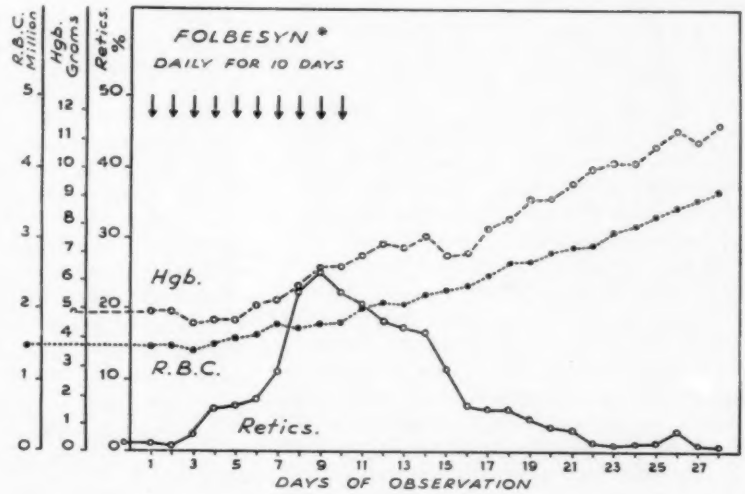

FIGURE 17. Hemopoietic response of a patient with nutritional macrocytic anemia to FOLBESYN®.

*Each injection of Folbesyn contains:

Vitamin B_{12}	5 mcg.
Folic acid	3 mg.
Riboflavin	10 mg.
Vitamin C	300 mg.
Thiamine hydrochloride	10 mg.
Pyridoxine hydrochloride	5 mg.
Sodium pantothenate	10 mg.
Niacinamide	50 mg.

found no patient who responded to the citrovorum factor who did not respond to folic acid.) When we administered the citrovorum factor, we chose to inject it although it is effective when administered orally. We believe, however, that in the stomach this compound is changed back to folic acid from which it was artificially synthesized.

SUMMARY AND CONCLUSIONS

By nutritive failure we mean a clinical condition which connotes the failure of an adequate supply of specific nutrients. It would appear that all tissues, and indeed all living things, require these nutrients for their normal functioning. As they function in our tissues, these vitamins are important in aiding the processes of repair so that those of decay may be overcome or re-

tarded. Persons whose eating habits are poor are apt to have trouble. The burdens of motherhood and of hard labor increase the need for these materials, and thus predispose to critical shortages. In the practice of medicine, mixed vitamin therapy has a definite, well earned and useful place.

How to use the vitamins to replenish the tissues is the physician's problem. We know these nutrients must be supplied to the body from the outside. If he has made a precise diagnosis and prescribed judiciously, even a short, intensive period of therapy will convince the most skeptical physician. It is our observation that large doses of materials should be prescribed at first, and that they should be prescribed by mouth, unless, for some reason, parenteral administration is necessary, as it sometimes is. Certainly the patient with pernicious anemia can be more surely protected if vitamin B_{12} is administered by injection rather than by mouth.

A freshly prepared sterile solution containing 15 micrograms of vitamin B_{12} concentrate and 5 mg. of folic acid in distilled water has been administered intramuscularly daily for 10 days to each of 5 patients with the following types of anemia in relapse: pernicious anemia with acute neural degeneration, nutritional macrocytic anemia, the macrocytic anemia of pregnancy, the macrocytic anemia of tropical sprue and the megaloblastic anemia of infancy. In each instance there was a prompt hemopoietic and clinical response. Except in the macrocytic anemia of pregnancy this response could have been produced by either the vitamin B_{12} or the folic acid in the preparation.

It has been shown repeatedly, however, that the macrocytic anemia of pregnancy is not relieved by vitamin B_{12} so that the response of the patients with this type of anemia should be attributed to the folic acid. The preparation was effective in relieving the symptoms arising from the nerve degeneration and the acute glossitis of pernicious anemia. Since it has been shown that such symptoms cannot be relieved by folic acid, their relief obviously was effected by the vitamin B_{12}.

Since 1945 we have been administering folic acid to patients with pernicious anemia and, since 1946, when we started a large series of patients on folic acid, a total of 80 patients has had folic acid for four or five years in doses ranging from 1 to 10 mg. each day. They also have had frequent injections of either liver extract or vitamin B_{12}, or both. None of these patients has developed neural degeneration, thus indicating that in the presence of vitamin B_{12} or substances containing vitamin B_{12}, such as refined liver extract, folic acid has in no way adversely affected the nerve tissue. It is well known that neural degeneration is an integral part of the pernicious anemia syndrome and that folic acid will not prevent its occurrence. It also has been demonstrated conclusively by our group and by other investigators that folic acid and vitamin B_{12} are essential in the treatment of certain types of anemia. They occur together in liver and some other natural foods, and it is well to prescribe them together in suitable doses. All patients with pernicious anemia should have parenteral injections of either vitamin B_{12} or liver extract. It is likely that liver extract and yeast contain many important nutrients not now identified.

In every paper we have written on this subject, we have stressed that vitamin therapy alone is not sufficient. The vitamins, however necessary, cannot take the place of a well balanced diet in restoring the tissues of a malnourished person. In the present practice of medicine the newer vitamins, which we have discussed at some length, play a most important role in blood-building. These vitamins, folic acid, vitamin B_{12} and its family, and the citrovorum factor, should be considered as nutritional factors as well as antianemic substances. The four principles of therapy which we have used so successfully in the rehabilitation of persons with various types of nutritional failure are:

1. Conditions causing excessive requirements for nutrients were removed or relieved whenever possible.

2. Symptomatic treatment and treatment for coexisting diseases were given.

3. It was made certain that the patient daily ate a diet which supplied 3000 to 4000 calories, 120 to 150 gm. of protein, and liberal amounts of minerals and vitamins.

4. Therapeutic substances, such as dried brewers' yeast powder, liver extract, or vitamins in the form of synthetic substances, were administered in sufficient amounts to correct the deficiency.

It cannot be expected that these four principles will be effective if the diagnosis is not precise or if they are not applied persistently.

Testosterone Propionate in Carcinoma of the Breast

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MAYO CLINIC, ROCHESTER

Testosterone propionate was administered regularly to patients with microscopically proved carcinoma of the breast. No evidence of permanent control of the disease was obtained. It is emphasized that treatment with hormones of this type should not be substituted for established procedures such as surgical measures or radiation.

THE purpose of this paper is to report on a series of patients who had microscopically proved carcinoma of the breast and who were given 300 mg. of testosterone propionate intramuscularly each week for a period of 52 weeks.

MATERIAL AND METHOD

The patients studied met one or more of the following criteria: (1) The grade of malignancy was 3 or 4 (of Broders' method), and there was axillary metastasis at the time of operation. (2) At the time of operation at the Mayo Clinic there was no demonstrable metastasis but, at a later date, a metastatic lesion or lesions were observed. (3) Operation was performed elsewhere and the patient later came to the clinic because of metastatic lesions. (4) At the time of initial physical examination, the patient was found to be suffering from inoperable lesions of the breast.

Sixteen patients who met these criteria were included in the study. Since it was necessary to re-evaluate the condition of these patients frequently, the majority of them lived in close proximity to Rochester, Minnesota. In each case, the patient or her relative was informed regarding the seriousness of her disease and care was taken to outline carefully the scope of the medication with stress on the untoward as well as the theoretic beneficial effects. Generally, the more conversant the patient or her relative was with these factors, the greater was the cooperation received in the study.

During the last 10 years, approximately 3500 patients have been operated on at the Mayo Clinic because of malignant disease of the breast. The limited number herein studied illustrates the careful screening which was necessary and also represents but a sampling of a larger series to be reported on at a later date.

Before the method is outlined by which the 16 patients in this series were studied, it might be interesting to note the availability, for long range studies, of patients having malignant lesions of the breast. Of 3,974 female patients who underwent radical mastectomy for unilateral carcinoma of the breast with metastasis, Harrington could find only 31.9 per cent who lived five years or more following operation. Of 2,659 who did not have metastasis at the time of operation, approximately 60 per cent were alive five years thereafter. By grouping both classes of patients—namely, those with and those without metastatic lesions of the lymph

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EDWARD A. BANNER

nodes at the time of operation (a total of 6,633 patients) only 50 per cent were found to be alive five years after operation. When they presented themselves for diagnosis, 63.9 per cent had axillary metastasis, and approximately 50 per cent of those with such metastasis had grade 3 lesions. One can see that the material for long range critical study is limited not only by geographic factors but also by individual longevity.

The method of studying these patients was uniform. It was planned to treat them with testosterone propionate alone, with the thought that if roentgen therapy were used for the metastatic lesions, the resultant evaluation would be equivocal. A general appraisal of the patient was made before therapy was begun. This included such pertinent data as age, menstrual history, gravidity, color of skin and any associated conditions such as diabetes, pregnancy, and so forth. The distribution and amount of hair were determined. Included in the initial evaluation were the duration of the disease, the breast involved and the location of the lesion in the breast, as well as the presence or absence of ulceration. The type of operation, name of the surgeon, the grade of the lesion and the number of lymph nodes involved metastatically were likewise noted. Certain laboratory studies preceded the administration of testosterone, such as roentgenographic examination of the chest, hemoglobin determination, erythrocyte and leukocyte counts, together with determinations of the sedimentation rate, serum calcium, phosphorus and alkaline phosphatase. Determinations of the urinary gonadotropins in women who had previously ceased to menstruate, estimation of the 17-ketosteroids, and photographs in appropriate cases were made.

After these initial determinations, the patient was asked to return every three months for re-evaluation. Previous to her dismissal, and at the initial return visit, the dosage and manner of administration of the drug were prescribed and the follow-up procedure explained. At each successive visit, the patient was examined by one of the consultants in the Section of Obstetrics and Gynecology. Observations were made regarding hirsutism, changes in the skin and voice, hypertrophy of the clitoris and peripheral edema. In appropriate cases, color photographs were routinely made in order to observe the changing character of soft tissue lesions. The patient was routinely questioned regarding relief of pain, reduction of disability, appetite, habits of sleep and alterations in libido. The described laboratory procedures were repeated and the results compared at each visit. Occasionally consultation with other consultants of the clinic was enlisted in order to evaluate more completely the patient's progress, with the purpose of ruling out any possible medical condition which might be attributed to the malignancy.

RESULTS

Of the 16 patients in the study, 8 were started on treatment with testosterone because of osseous metastasis. In a period of 12 months, each patient continued to have additional metastatic growths in other parts of the skeleton although some presented roentgenologic evidence of recalcification from time to time. Seven of the 16 patients presented soft tissue metastasis when administration of testosterone was begun; 1 of the 7 patients had what was thought to be a pulmonary metastatic lesion. In this patient, complete remission of the lesion was noted and the findings on subsequent roentgenographic ex-

amination of the chest were within physiologic limits. Since no tissue was obtained from this pulmonary lesion for biopsy, the possibility of roentgen misinterpretation might be entertained. The remaining 6 patients with soft tissue metastasis showed no evidence of healing of the soft tissue lesion although, in a few, progression of growth seemed to be definitely limited. One of the 16 patients presented evidence of both osseous and soft tissue metastasis; during a 12 month period, progression in her lesions was the rule.

Subjectively, all the patients exhibited some degree of euphoria while under treatment and the majority gained weight. Whether this was due to increased appetite, the protein-sparing properties of androgens or hidden edema as a result of sodium retention cannot be said. However, it was noted by independent observers that each patient generally felt much better and acquired a definite feeling of well-being. This was not sustained over a period of one year in all individuals. In a few patients, water retention became pronounced and in some elderly patients congestive heart failure was noted.

The blood picture assumed some unusual patterns, for although these patients were all drastically ill with the majority progressing rather rapidly toward death, the value for hemoglobin generally increased. Four of the 16 patients had an increase of 2 gm. or more in hemoglobin value over a period of 52 weeks while the remaining 12 patients, with one exception, exhibited lesser increase. A proportionate increase in the number of erythrocytes was likewise noted, with some patients having gains of as much as one million cells. None of these individuals was receiving a preparation of iron during the indicated period of observation. The leukocyte count varied to such an extent that mean values were not significant. Although the sedimentation rate was invariably above what one might expect for a normal person, it was of no prognostic value. In many determinations, a lowering of the rate toward normal was observed in the face of rapidly developing metastatic lesions. In others, marked fluctuations were noted when the physical condition appeared stationary.

No significance could be attached to the values for calcium, phosphorus or alkaline phosphatase. Certain investigators have noted calcification of osteolytic skeletal metastatic lesions and have reported a reduction in the value for serum calcium. They have interpreted this decrease as evidence of the deposition of calcium in the bone. My colleagues and I have not noted this correlation although in some patients a decrease in this value was observed. Others have sought a further index of metastatic activity by noting the value for alkaline phosphatase. It was reasoned that an increase in the quantity of alkaline phosphatase in the blood accompanied calcification of skeletal metastatic lesions which were osteolytic. Since such fluctuations are dependent upon activity of the osteoblasts, an increase in the quantity of alkaline phosphatase in the blood either may be indicative of a reparative process following osteolytic metastasis or it may represent new osteoblastic metastasis, or a combination of both. Thus such an increase in alkaline phosphatase, when observed, may actually mean more metastasis rather than comforting repair.

A train of untoward subjective symptoms after the use of androgens is more easily prophesied. These depend more on the age of the patient than on the dose employed, and are seen less frequently in patients who have reached an age of 60 years or more than in younger persons. It has been estimated that more than 200 mg. of testosterone propionate per month is required to produce masculinization and cessation of menstruation in women during the reproductive years. In such patients, an excess of hair on the face, body and extremities is a fairly consistent finding. Daily shaving of the face is not unusual, although this seems to be a bothersome feature more frequently in the brunette than in the blond patient. After cessation of treatment the excess growth of hair does not readily disappear. Some patients have resorted to electrolysis with some success, but this is expensive and time-consuming. Acneform eruptions frequently accompany the excess growth of hair and a distinct oiliness of the skin may be noted. The younger the patient, the more readily one notices the lowering of the voice in the course of androgenic therapy. This is first described as a hoarseness, and is thought to be the result of an actual anatomic change in the larynx and thyroid cartilages. After cessation of androgenic therapy there is some return to normal but the voice generally remains harsh.

A marked increase in sexual urge is a frequent unpleasant side effect. It occurs among

almost all patients receiving testosterone propionate except those of the older age group. This increase in libido is often accompanied by an enlargement of the clitoris, with a decided increase in its sensitivity. The engorgement may interfere with the patient's sleep and sometimes an anesthetic ointment is required to alleviate this difficulty.

Little has been written concerning sensitivity to the drug, but where sensitivity has been noted it has been characterized mainly by nausea and vomiting and, in some persons, by severe pruritus. Infrequently there is an unpredictable rise in serum calcium. This is followed by listlessness, nausea, vomiting and, according to some reports, death. An antidote, intravenous administration of 2.5 per cent solution of sodium citrate, and discontinuance of androgenic therapy are suggested when the above symptoms are noted.

It is apparent that testosterone propionate in the described doses profoundly influences the hormonal status of the individual. One is intrigued by the variability of responses in individual patients under apparently similar circumstances. The natural course of malignancy of the breast must be taken into consideration when evaluating the efficacy of any drug in its treatment, and there is no evidence to show that any medication is a cure although some drugs seem of inestimable value as palliative agents. Each patient must be individualized, for in some the untoward reactions far outweigh the theoretic beneficial effects.

SUMMARY

The clinical records of 16 patients who received testosterone propionate for 52 weeks are reviewed. At the clinic no evidence has been found to indicate that sex hormones will result in permanent control of cancer of the breast. It should be stressed that such hormones should not be substituted for established procedures such as surgical measures or radiation, but they may be of distinct value as palliative agents.

PATHOLOGY AND POLITICS

TWO INTERESTS—the study of pathology and the study of economic and social problems—were of foremost importance in the life of Rudolf Ludwig Karl Virchow (1821-1902). Fortunately for the medical world, the second interest did not overshadow the first, and during his long and distinguished career, Virchow made many basic contributions to medical progress.

Virchow was born in Pomerania, attended the gymnasium at Koslin and started his medical studies at the Kaiser Wilhelm Akademie; he received his degree from the University of Berlin in 1843. When he was appointed Privatdozent in Pathology in 1847, he began the work which was to bring him fame and honor.

Offered the chair of pathology at the University of Berlin in 1858, Virchow accepted with the proviso that the government build him a new pathologic institute. Shortly thereafter, he published his noted treatise on *Cellularpathologie* which contained the precept now known as Virchow's law—all cells are derived from pre-existing cellular elements—stated in the Latin phrase in Edmund Kopietz' cover painting.

In addition to his activities in medical research and teaching, Virchow also served in the Reichstag for 13 years, being leader of the Radical party during that time.

Developmental Diagnosis of Infant Behavior

ARNOLD GESELL*

YALE UNIVERSITY SCHOOL OF MEDICINE, NEW HAVEN

The general practitioner and the pediatrician are devoting an increasing proportion of their professional time to the protection of health in children who are not sick. This demands a clinical technic for the diagnosis of normal development and the early detection of developmental defects and deviations. A screening method of behavior inventory is outlined. A color motion picture film demonstrated the principles and procedures of the developmental examination of infant behavior.

WILLIAM OSLER in one of his apt phrases suggested that pediatrics is the specialty of general medicine. And so it is. By the same token, the general practitioner is a pediatrician when he serves children, and that service often exceeds one third of his clinical case load. A recent survey by the American Academy of Pediatrics shows that over 60 per cent of the pediatrician's professional time is devoted to the care of children who are not sick.

Pediatrics is steadily becoming a supervisory type of preventive medicine, concerned with the systematic protection of the total child—in sickness and in health, physically and mentally. All children, whether normal or handicapped, are confronted with the universal problem of growing up. Health in a growing child must be defined, therefore, as that condition which permits and promotes optimal development, which means, does it not, that development as well as disease now falls within the scope of clinical pediatrics and of general medicine.

Parents sense this fact. One question is always in the background of their minds when their child comes to the attention of the doctor: Is our child developing as he should? If the child is retarded or suffers from some handicap, the question becomes doubly anxious and insistent. And the question deserves an answer.

ARNOLD GESELL

Development does not take care of itself altogether. It needs diagnosis, it needs supervision, often it needs clinical guidance—particularly throughout the first five years of life. Every child is born with certain undetermined growth potentials. As he matures he manifests these potentials in three major signs and symptoms:

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Presented at the thirty-fifth (Chicago) annual Assembly of the Interstate Postgraduate Medical Association.

FIGURE 1. Illustration from an animated section of the motion picture film depicting *The Embryology of Human Behavior. Narration:* "Behavior patterns are forming. The patterning process begins long before the infant is born—even in the darkness of the uterus . . . In the embryo, one lunar month after conception, brain, eyes, and hands are already taking form. The heart soon begins its rhythmic life-long beat . . ."

in his anatomy, in his physiologic functions and in his behavior. The behavior signs are of pre-eminent importance because they are the most authentic index of the child's maturity and also of his constitutional make-up. Here is sound ground for constitutional medicine. A man may be as old as his arteries, but an infant is as old as his behavior.

Fortunately the behavior signs yield to observation and to diagnostic examination. The growing mind of the infant is not concealed; it reveals itself in actions, in behavior patterns open to inspection. The patterns assume characteristic shapes which unfold from age to age in lawful sequence.

At four weeks the infant lies with his head averted, staring into space—a postural pattern of behavior. At 12 weeks he looks at his hand—an adaptive pattern, the beginning of eye-hand coordination. At 28 weeks he grasps and can pick up an object promptly; attention does not now oscillate between his own hand and the object; he picks it up directly on sight, transfers it from one hand to the other, with increasing eye-hand coordination. At 40 weeks he can reckon with two objects and bring them together combiningly. Intelligence really is growing. At one year he can take one object after the other, pick up one, release it, pick up the next, release it, pick up and release one by one in a serial order—the embryonic beginning of counting and also evidence of voluntary control. All the time he is exhibiting an expanding repertoire of action patterns in postural, motor, perceptual, language and personal-social fields of behavior (Figures 3, 4, 5 and 6).

At the Yale Clinic of Child Development we have charted the behavior characteristics typical of 34 advancing age levels from birth to the tenth year. The varied behavior items have been classified into growth gradients and codified into condensed developmental schedules. These graded schedules serve as normative criteria for the diagnosis and appraisal of infant behavior.

The methods of examination are simple. Test objects which have play interest for the child are presented on a test table in an examining crib, very much like an ordinary hospital crib. The behavior tests evoke behavior patterns. Each pattern is noted, recorded and assessed on the basis of its maturity value. We do not attempt to derive a bare I.Q. A developmental diagnosis aims to formulate the organization and the functional integrity of the total action system, mainly the neuromuscular system (Figure 6).

Expertness in the technic of developmental examination, reinforced by clinical insight, may require one or two years of postgraduate training in connection with an active diagnostic

FIGURE 2. *Early fetal stage* (excerpt from film). *Narration:* "In two months the embryo becomes a fetus. The fetus is capable of small almost imperceptible movements—flexor movements of trunk and shoulders."

service, embracing both normal and deviating children. It is, however, possible for the untrained and the self-trained physician to apply selected behavior tests in a simplified inventory manner as a minimum check and as a screening device for detecting possible abnormalities.

I believe that the general practitioner should not depend quite so much on intuition and casual impressions, but should deliberately take some moments of time to elicit behavior patterns and to assess them as evidence of the child's developmental maturity.

For over a year now I have been working with a technical team on the production of a motion picture film which has now been completed, the purpose of which is to present the principles and methods of developmental diagnosis. The film is entitled "The Embryology of Human Behavior," because "embryology" is a word that goes to the heart of the matter. Embryology is the science of development, and the film is designed to demonstrate the developmental continuity of prenatal and postnatal behavior.

The procedures of developmental diagnosis are based on a knowledge of the normal sequences of behavior patterning. The film illustrates how these procedures may be used in infancy for routine inventory and also for the differential diagnosis of normality, mental deficiencies, cerebral palsy, neurologic impairment and other forms of maldevelopment.

This is a conceptual rather than a documentary film. As such it was sponsored by the newly established Medical Film Institute of the Association of American Medical Colleges and produced in cooperation with the Bureau of Medicine and Surgery of the United States Navy and the Office of Naval Research.

The film extends the concepts of embryology to include the action system of the child as manifested in patterns of behavior both before and after birth. He grows as a unit. The body grows. Behavior grows. The film depicts behavior patterns which are characteristic of normal mental growth.

IN his pediatric capacity, the general practitioner of today is called upon to keep a watchful eye on the mental as well as the physical growth of his young patients. The film may give him some hint as to how he can apply simple behavior tests to determine normality or to detect neurologic impairments and faulty development. The accompanying schedule (Table 1) is

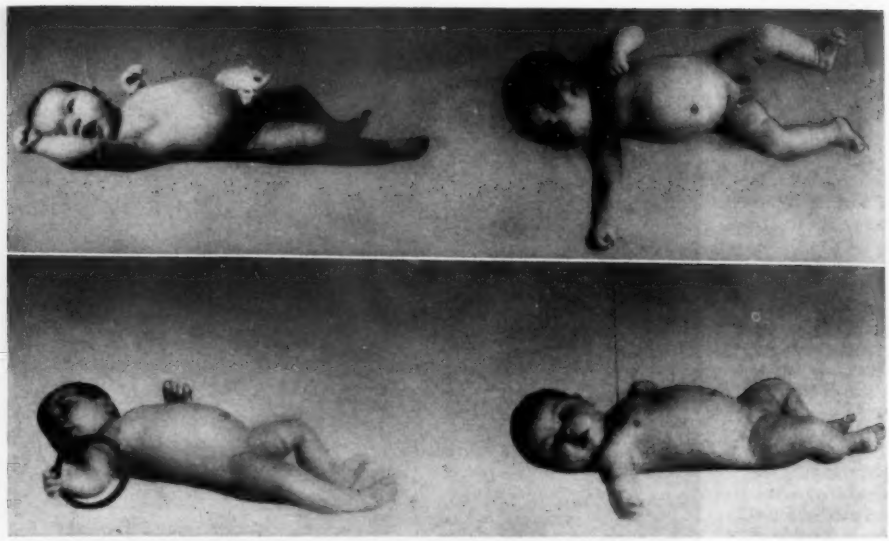

FIGURE 3. *Early postural patterns.* The tonic-neck-reflex pattern is pictured in a normal infant at 1, 6, 8 and 12 weeks of age. The infant lies with head averted to one side, the arm on that side extended, the opposite arm flexed near the shoulder. This asymmetric attitude leads to eye-hand coordination. It is so basic for sensorimotor development that it is present in rudimentary form in the fetal infant, born some 10 weeks prematurely.

This pattern has clinical significance in the diagnosis of developmental status. If it persists markedly beyond the first six months, it denotes amentia or neurologic defect.

FIGURE 4. *The symmetro-tonic-reflex pattern* in the same infant at 20 to 24 weeks of age. Asymmetry gives way to symmetry of postural attitude. The head now prefers the midplane and the hands close in upon a proffered object (a cube)—the beginning of elementary prehension. With coordination of eyes and hands the infant reaches and grasps on sight.

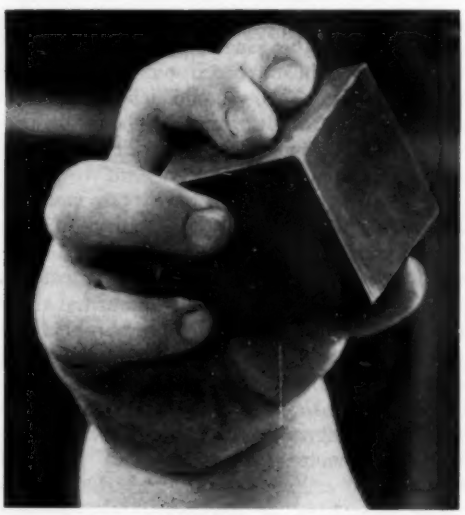

FIGURE 5. *Perfected prehension at 1 year of age.* Early grasp is crude and palmar. Later grasp is digital with increasing specialization of the radial digits. The year old infant grasps the cube with thumb opposition, as shown by this close-up from the film on *The Embryology of Human Behavior.*

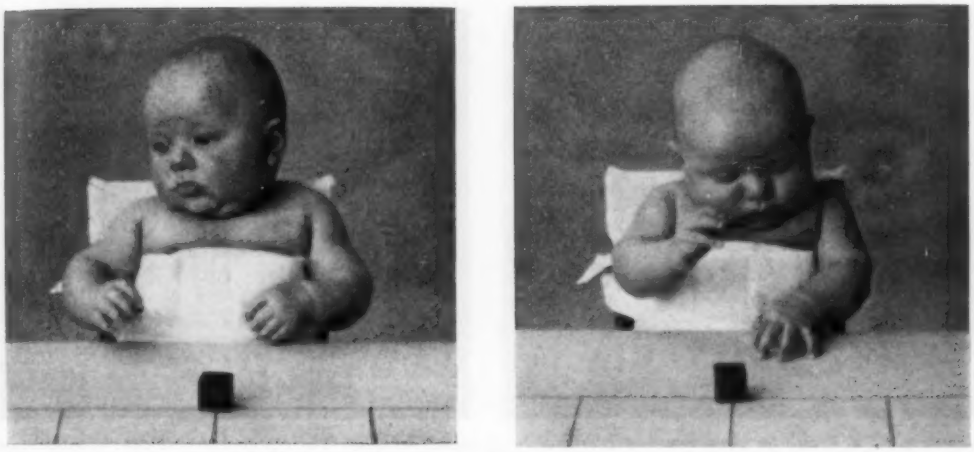

FIGURE 6. *Eye-hand coordination in the making.* The eyes take the lead over hands in development. The infant at 16 weeks reaches with his eyes, but not with his hands. He looks at surroundings; he looks at his hands, and at the cube. He can not grasp the cube on sight.

TABLE 1

PRELIMINARY BEHAVIOR INVENTORY

Name		*Age*	*Date*	*Case No.*
AGE ZONE	MOTOR	ADAPTIVE	LANGUAGE	PERSONAL-SOCIAL
4 wks.	Lacks head control	Brief eye-following	Impassive face	Stares at surroundings
	Asymmetric in supine	Drops toy immediately	Small throaty sounds	"Listens" to sound
16 wks.	Head erect, slight bobbing	Incipient approach, rattle	Coos	Spontaneous social smile
	Symmetric supine postures	Regards rattle in hand	Laughs aloud	Hand play
28 wks.	Sits, leaning forward	Reaches and grasps toy	Squeals	Feet to mouth
		Transfers toy	m-m sound (crying)	
40 wks.	Sits well, creeps	Combines 2 toys	Dada-Mama	Nursery tricks
	Pulls to feet at rail	Picks pellet, thumb and index	One other "word"	Feeds self cracker
52 wks.	Walks, one hand held	Cube into cup	Two other "words"	Cooperates in dressing
		Tries tower 2 cubes	Responds "Give it to me"	
15 mos.	Walks alone, toddle	Tower, two cubes	4-6 words	Points and vocalizes wants
		Six cubes into cup		Casts toys
18 mos.	Walks well alone	Tower 3-4 cubes	10 words	Toilet regulated, day
	Seats self, small chair	Imitates a stroke |	Jargon	Carries, hugs doll
2 yrs.	Runs	Tower 6-7 cubes	Joins 2-3 words	Asks for toilet, day
	Up, down stairs alone	Imitates circular scribble	Names 3-5 pictures	Puts doll to bed, etc.
3 yrs.	Rides tricycle	Imitates "house" of cubes □□	Sentences	Feeds self well
	Stands 1 foot, momentarily	Imitates cross +	Gives full name, sex	Puts on socks, unbuttons

INSTRUCTIONS: (1) Check the most advanced behaviors in *each field of behavior.* (2) The checks will indicate an *approximate* maturity age zone. (3) *No diagnosis can be made on the basis of this inventory.* Gross deviation from actual age, or marked disparity between behavior fields, indicates the need for a diagnostic behavior examination.

CHARACTERIZATION: (Physical factors, social factors, posture, attention, rapport, emotion, speech, etc.)

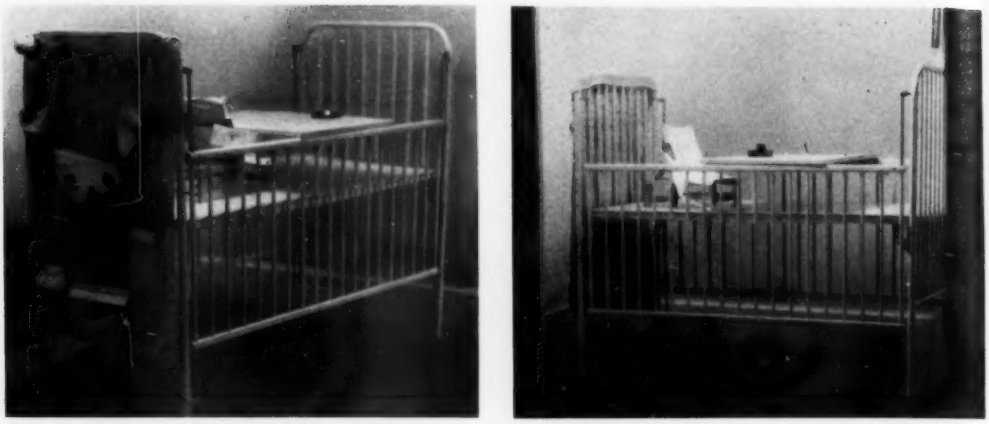

FIGURE 7. *Clinical crib for developmental examination of infant behavior.* The equipment includes an assortment of test materials—cubes, bell, etc., a test table top which rests on the adjustable side panels, and a small examination chair also pictured in Figure 6. A one-way vision screen partition which permits concealed observation is shown. A simple examination unit of this kind is a serviceable device in pediatric and general practice.

so constructed that it requires no more than several check marks for the maturity items listed for nine age zones. This schedule enables the physician to make a simple routine record of infants under supervision at home, in hospitals, child-caring institutions and outpatient clinics.*

The inventory is only approximate and preliminary. It is based on age zones rather than precise maturity levels. It is in no sense a developmental examination nor a substitute for such an examination. The inventory is intended to serve as a selective screening device and to indicate those cases which especially need formal behavior examination. Periodically undertaken by the supervising physician, a simple inventory may become a valuable part of the history record of the child, particularly if untoward developments occur in later life. Repeated inventories take on increasing diagnostic value and have significance for presumably normal children as well as for children who present defects and deviations.

Nine age zones are represented in the inventory with one or two maturity items for each of the four major fields of behavior in each zone. In making the inventory it is important to cover *all* of the fields of behavior and to note whether there is a marked disparity within the four fields with scatter over a wide range of ages. If the check marks gravitate consistently to an age zone which is one full interval below the chronologic age of the child, some retardation is probably indicated.

Each schedule carries a blank space for comment and supplementary observations. These observations may cover emotional characteristics, a brief characterization of atypical behavior and any unusual behavior events. The record also may make reference to behavior items of favorable import. The function of a routine behavior inventory is to keep the clinical problems of development in focus.

*For fuller details see pages 402 to 408 of GESELL, A. and AMATRUDA, C. S.: Developmental Diagnosis: Normal and Abnormal Child Development, Clinical Methods and Pediatric Applications, Enlarged Edition 2. New York, Paul B. Hoeber, Inc., 1947.

Diagnostic Clinic

Lesions of the Adrenal Glands and Pancreas

WALTMAN WALTERS*

MAYO CLINIC AND MAYO FOUNDATION, ROCHESTER

LESIONS OF THE ADRENAL GLAND

It is my privilege and pleasure today to present some interesting cases to you. The first patient is one with a hyperfunctioning lesion of the adrenal cortex. The young lady was presented to you by Dr. Willard Thompson a few days ago briefly to illustrate some of the points which he wanted to make at that time. She is such an excellent patient and is so characteristic of a group of patients with hyperfunctioning lesions of the adrenal cortex that the young lady and Dr. Thompson very kindly have come here and we will try to put on a little combination clinic for you, and then if the time permits we will discuss briefly some lesions of the pancreas.

Dr. Thompson, we would appreciate it very much if you would be kind enough to give this patient's history.

DR. WILLARD O. THOMPSON (Chicago): The essential feature of the patient's problem is that she has a masculinizing process. There appears to be no doubt that the cause of this is overproduction of androgen by the adrenal cortex. She is now 10½ years old. This alteration was first noticed at the age of 6 years, when pubic hair and growth of the clitoris appeared.

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Presented at the thirty-fifth (Chicago) annual Assembly of the Interstate Postgraduate Medical Association.

DR. WALTERS: Dr. Thompson has spoken about the hirsutism or the abnormal growth of hair. This child has hair on her chin and she has a little on her chest, and if you look at her thighs and legs, you see a hirsuties there. You will note also that she has a male escutcheon to her pubic hair line.

DR. THOMPSON: It is interesting that no uterus is present, there is no cervix and no vagina. However, she does have two ovaries and two fallopian tubes. The urethral opening is in the usual feminine location. There is no testicular tissue. All of the androgen comes, so far as we can tell, from the adrenal cortex.

DR. WALTERS: May I interrupt you again? Dr. Thompson has spoken about the androgen coming from the adrenal cortex. Why is that? The cortex of the adrenal glands, ovaries and testes embryologically each take their origin from the urogenital ridge. Therefore you will find frequently some of these same signs to which Dr. Thompson has referred not only with hyperfunction of the adrenal cortex but with the ovarian arrhenoblastoma and sometimes with the feminizing tumors of the testes.

DR. THOMPSON: A photograph of this patient taken about a year ago shows the enlargement of the clitoris and the growth of pubic hair. Since this was taken her masculinization has become more complete, her muscles are like those of a male, her bone age along with this

WALTMAN WALTERS

overproduction of androgen has increased very rapidly, and at the present time practically all of her epiphyses are closed at the age of 10½, so that her bone age is greatly advanced as a result of this precocious or premature and abnormal overproduction of androgen. Those are the main things, Dr. Walters.

DR. WALTERS: Dr. Thompson, I assume that you have excluded a masculinizing tumor of the ovary with the exploration?

DR. THOMPSON: Yes.

DR. WALTERS: Since this patient has no testicular tissue, what do you think is the basis of her syndrome?

DR. THOMPSON: I think she has hyperplasia of the cells of the adrenal cortex that produce androgen. Both of her adrenals were explored in 1947 and no tumor was found at that time. Her excretion of 17-ketosteroids has varied from about 22 to 45.

DR. WALTERS: I would like briefly to review some of the important features relating to the adrenal gland. It is a gland which you must learn about. You have heard Dr. Thompson say that the adrenal glands of this patient were explored surgically and there were no tumors present.

What other method is there of viewing the adrenal glands? Cahill[1] of New York has been successful in some cases in making the shadow of an enlarged adrenal gland visible in a roentgenogram, especially if there is a tumor, by the injection of air around the adrenal gland. I tried this a few years ago in several cases, but the shocklike reactions so frightened me that I would not continue to carry on that test. Moreover, it was my opinion that exploration of the glands, which can be done as easily as one can explore the kidney, in fact more easily, enables one to determine more accurately whether or not even a very small tumor is present. I have not seen any aerograms outlining the adrenal glands which conclusively proved the presence of small tumors. Moreover at exploration the surgeon can resect portions of one or both glands if advisable.

We will briefly go over some of the diseases of the adrenal gland. I want to call attention to the fact that when you have a lesion of the adrenal cortex, bear in mind what I said, that it takes its origin embryologically from the same structure that gives rise to the ovaries and the testes, and precocious puberty will develop in the child. In the adult female, hyperfunction of the cortex due to a tumor of the adrenal cortex or to a disturbance within the pituitary gland which stimulates the cells of the cortex of the adrenal gland produces amenorrhea and a buffalo type of obesity in addition to the signs which you have seen displayed in the patient shown here. My colleague, Dr. Randall Sprague, and I have recently published studies on several such cases.[2,3]

Since the medullary portion of the adrenal gland takes its origin from the same structures which give rise to the sympathetic nervous system, tumors of the adrenal medulla are characterized by paroxysmal attacks of hypertension, and the most frequent tumors taking their origin from the medullary substance are the pheochromocytoma and the neuroblastomas. The latter have been recently studied by one of my colleagues, Dr. Poore.[4]

The adrenal cortical tumors, as well as the adrenal cortical hyperplasia or hyperfunction, in boys produce homologous sexual and somatic precocity. By that we mean that the genitalia develop as though the male child had reached puberty or beyond. Young girls likewise have a homologous somatic and sexual precocity, by

TABLE 1

ACTIVE COMPOUNDS ISOLATED FROM THE ADRENAL CORTEX*

COMPOUND	EFFECT	CLINICAL SYMPTOMS AND SIGNS WHICH MIGHT RESULT FROM OVERPRODUCTION†
1. Desoxycorticosterone	Salt and water metabolism	Retention of salt and water—edema, hypertension and congestive heart failure; increase in urinary content of potassium; profound muscular weakness
2. 17-hydroxy-11-dehydrocorticosterone (compound E) 11-dehydrocorticosterone (compound A) Corticosterone (compound B) 17-hydroxycorticosterone (compound F)	Carbohydrate and protein metabolism	Negative nitrogen balance, thinning of skin, muscular wasting and weakness, osteoporosis, ecchymosis, diabetes, lymphopenia, eosinopenia
3. 11-dehydrocorticosterone (compound A) Corticosterone (compound B)	Fat metabolism (?)	Obesity (?)
4. Androstenedione 11-hydroxy-isoandrosterone Adrenosterone 17-hydroxyprogesterone	Androgenic effect	Virilism: hirsutism, baldness, amenorrhea, florid skin, hypertrophy of clitoris, acne, masculinization of habitus and voice in women, sexual and somatic precocity in children
5. Estrone	Estrogenic effect	Vaginal bleeding and sexual precocity in female children; impotence and gynecomastia in men
Progesterone	Progestational effect	

*The table is taken with modifications from Kepler, Sprague, Mason and Power.[8]
†The fact that recently numerous symptoms and signs reminiscent of Cushing's syndrome have been induced in patients with large doses of compound E (17-hydroxy-11-dehydrocorticosterone) may call for some revision of present concepts of the pathogenesis of Cushing's syndrome.

which is meant that they likewise have a precocious development of the breasts and genitalia. I have operated on infant female children[5,6] who had menstruated and who had hypertrophy of the breasts. In men (and it is a very rare lesion in men) heterologous changes of feminization occur, that is, enlargement of the breasts takes place, there is disappearance of whiskers from the face and hair from the body and a decrease in the size and the consistency of the testes. These changes revert to masculine conformations when the adrenal cortex tumor is removed.

The formulas of these steroids are complex (Table 1). It is necessary that we become somewhat acquainted with these compounds and their metabolic activities and effects. We have heard much of compound E of Kendall, or cortisone, of late. As was brought out so admirably by previous speakers, the effects of Kendall's compounds E, A, B and F are their effects on carbohydrate and protein metabolism.

The steroid, 11-dehydrocorticosterone, probably also has an effect on fat metabolism.

How many steroids are there, Dr. Thompson?

DR. THOMPSON: Twenty-eight have now been isolated.

DR. WALTERS: Associated clinical and chemical problems of this sort—and that is why I wanted to have Dr. Thompson here—are quite complex usually for the clinical surgeon, even though he has a real interest in chemistry and physiology. I, therefore, would urge you to meet with your associates and friends, the surgeons, the physiologists and the practitioners of medicine, and go over these things together. Then record them on a card which you carry in your pocket where you can pull it out and look at them. These steroids are very important and you should know them and their relation to abnormal physiologic changes.

In Table 1 also are listed the clinical signs of overproduction of desoxycorticosterone acetate: that is, retention of salt and water, increased urinary excretion of potassium and muscular weakness.

Compound E, cortisone, also affects the metabolism of carbohydrate and protein; note also compound F, or 17-hydroxycorticosterone and what it does.

Some of the most interesting effects which are so characteristic of the hyperfunctioning lesion of the cortex are the hirsutism, the baldness in females, the amenorrhea, the florid skin, the hypertrophy of the clitoris, acne, masculinization of voice, sexual and somatic precocity (Table 2).

(To the patient): You didn't mind coming up here today?

PATIENT: No.

FIGURE 1. Child aged 23 months; adrenocortical tumor removed March 23, 1937. Dimensions, 5.5 by 4.5 by 4 cm.; weight, 45 gm.

DR. WALTERS: What grade are you in?

PATIENT: Fifth.

DR. WALTERS: Do you play baseball?

PATIENT: Yes.

DR. WALTERS: I wanted you to hear her low-pitched voice. Dr. Thompson's slide of the child's face and back showed the acne of the face, hypertrophy of the clitoris and, of course, somatic precocity. Sexual precocity as related to the uterus is not present because the uterus is absent.

Some of these youngsters have a perfectly typical small body of an adult, with adult hirsuties and enlargement of the breasts. It is easy to remember these things about adrenal tumors if you remember from what part of the gland the tumors take their origin.

FIGURE 2. (Same case as Figure 1.) Adrenal tumor.

TABLE 2

SYMPTOMS OF TUMORS OF THE ADRENAL CORTEX*

1. Non-endocrine symptoms

2. Symptoms dependent on age and sex
   - Boys: Homologous sexual and somatic precocity
   - Girls: Sexual and somatic precocity, usually heterologous; sometimes uterine bleeding and enlargement of the breasts
   - Men: Feminization
   - Women: Varying degrees of virilism

3. Symptoms independent of age and sex
   - Altered habitus
     - Facial and abdominal obesity
     - Kyphosis
     - Thin arms and legs
   - Purplish striae and ecchymoses
   - High color
   - Hypertension
   - Osteoporosis
   - Diabetes
   - Acne
   - Polycythemia
   - Hypochloremic alkalosis
   - Purpuric ecchymoses
   - Fatigue
   - Muscular atrophy

*The table is taken with slight modification from Kepler, Sprague, Mason and Power.[8]

I performed the operation in this group of cases within the last few years (Table 3). The excretion of 17-ketosteroids and corticosteroids is shown before and after operation. I wanted to include this table also so that you may note that there were 2 patients with Cushing's disease with hyperplasia of the adrenal glands (cases 7 and 9 of Table 3). The stimulus probably started in the pituitary and acted through

TABLE 3

TYPE OF CLINICAL SYNDROME, PATHOLOGIC DIAGNOSIS, EXCRETION OF 17-KETOSTEROIDS AND CORTICOSTEROIDS AND RESULTS OF DEXTROSE TOLERANCE TESTS IN 9 CASES

CASE	AGE, YEAR AND SEX	CLINICAL SYNDROME	PATHOLOGIC DIAGNOSIS; LESION OF ADRENAL CORTEX	TIME OF TEST	17-KETOSTEROIDS, MG. PER 24 HR.	CORTICOSTEROIDS, MG.	DEXTROSE TOLERANCE
1	62M	No endocrine manifestations	Adenocarcinoma, gr. 3, 2,685 gm.	No examination of urine for excreted hormones			
2	27F	Adrenogenital syndrome	Carcinoma, gr. 2, 25 cm. in diameter	Before operation	241.0 average for 3 days	.....	Diabetic curve
				Immediate p.o. period	2.1 average for 10 days	.....	
				4 mo. p.o.	10.3	.....	
				11 mo. p.o.	8.6	.....	
				24 mo. p.o.	7.0	.....	
3	45F	Adrenogenital syndrome	Adenocarcinoma, gr. 3+, 460 gm.	Before operation	170.0	.....	
				2 days p.o.	<1.0	.....	
				14 days p.o.	6.9	.....	
4	24F	Cushing's syndrome	Adenocarcinoma, low gr. 1, encapsulated, 10.5 gm.	Before operation	7.3	1.101	Diabetic curve
					3.5	.....	
				4 occ. in 1st 4 wk. p.o.	2.9; 1.0; 0.7; 1.1	.....	
				3 wk. p.o.	...	0.563	
				6 mo. p.o.	1.6	.....	
5	15 mo. M	Mixed picture	Adenocarcinoma, gr. 2, 40 gm.	Before operation	4.1	.....	
				Immediate p.o. period	0.2	.....	
				9 mo. p.o.	0.2	.....	
6	42F	Mixed picture	Adenocarcinoma, gr. 3, 100 gm.	Before operation	3.2	1.04	Diabetic curve
				p.o.	0.5	0.438	
					2.1	.....	
7	50F	Cushing's syndrome	Hyperplastic adenoma, 7.25 gm.	Before operation	4.9	1.59	Diabetic curve
					6.7	.....	
				Immediate p.o. period	0.9	.....	
					0.7	0.25	
				5 mo. p.o.	1.6	0.35	Normal curve
8	40 mo. F	Mixed picture	Carcinoma, gr. 2, 36 gm.	3 mo. before operation	6.2	.....	
				Immediately before operation	6.8	.....	
				10 days p.o.	0.3	.....	
				9 mo. p.o.	0.0	.....	
9	32F	Cushing's syndrome (incomplete)	Cellular adenoma, 8 gm.	Before operation	2.4	3.31	
				Immediate p.o. period	2.2	.....	

the cortex of the adrenal gland in order to produce the syndrome. Those patients with the tumors had a higher excretion of 17-ketosteroids in the urine than did those with Cushing's disease.

Dr. Thompson, do you find that characteristically true or not?

DR. THOMPSON: Yes. I think there isn't any doubt about that, Dr. Walters.

DR. WALTERS: You, I take it, regard the increased excretion of 17-ketosteroids in these cases as an important diagnostic sign, is that correct?

DR. THOMPSON: I think it is the single most important laboratory test whenever there is any question of any masculinizing effect from the adrenal cortex.

DR. WALTERS: Look at the excretion of the 17-ketosteroids in cases 2 and 3 (Table 3). You

FIGURE 3 *(left)*. Girl aged 3 years. Operation, April 14, 1942. Excision of right adrenal gland and associated tumor mass. Pathologic diagnosis of semicapsulated, hemorrhagic, degenerating adenocarcinoma grade 3+ of the adrenal cortex. Recurrence August 10, 1942; roentgenogram of the thorax showed multiple metastatic lesions.

FIGURE 4 *(right)*. Preoperative condition.

note how after the removal of the tumor there was a decrease to normal or nearly normal. In case 7 after a subtotal resection of the adrenal gland for Cushing's syndrome a satisfactory drop occurred too.

I SPOKE of the subtotal resection of the adrenal gland in Cushing's syndrome. Why, if there is no tumor and the glands do not appear to be enlarged, can regression of these symptoms be accomplished by subtotal adrenalectomy? The reason is that the pituitary cannot act through the adrenal gland if there is only a small amount of adrenal gland present. Perhaps many of you noted that interesting article[7] in the *Journal of the American Medical Association* on subtotal adrenalectomy for hypertension. The authors reported that all but about 5 per cent of the total quantity of both adrenal glands was removed in the treatment of hypertension. We have performed subtotal removals of the adrenal gland in a series of 28 cases for the treatment of Cushing's disease. I cannot get my colleagues in the department of metabolism to commit themselves yet as to the permanency of the result. Suffice it to say that sometimes remission of signs and symptoms occurs spontaneously, in which case it would appear that the patient was over the masculinizing effects or the feminizing effects of the adrenal cortical hyperfunction, only to have, as we have had in one of our young patients who had a subtotal adrenalectomy, a return of symptoms after a two year regression. That is why I think we must be careful indeed in evaluating the results of subtotal adrenalectomy in the treatment of Cushing's syndrome. The theory underlying the operation I have explained to you.

The risk of operation when there is a tumor is practically nil, because you can compensate and should compensate at the time of operation and immediately afterward for that lack of adrenocortical substances due to the removal of the tumor which has been giving off such a tremendous amount. This is done by giving either the whole gland extract or, as we have recently been trying, cortisone alone.

It is important not to be content with one postoperative evaluation of these excretions of 17-ketosteroids. I think the management of the hyperfunctioning adrenal gland whether by roentgen therapy to the pituitary or by subtotal adrenalectomy should still be considered in the stage of clinical investigation. We believe that these cases should be carefully followed for a long time after any type of therapy is done.

Figures 1 and 2 show a child 23 months old.

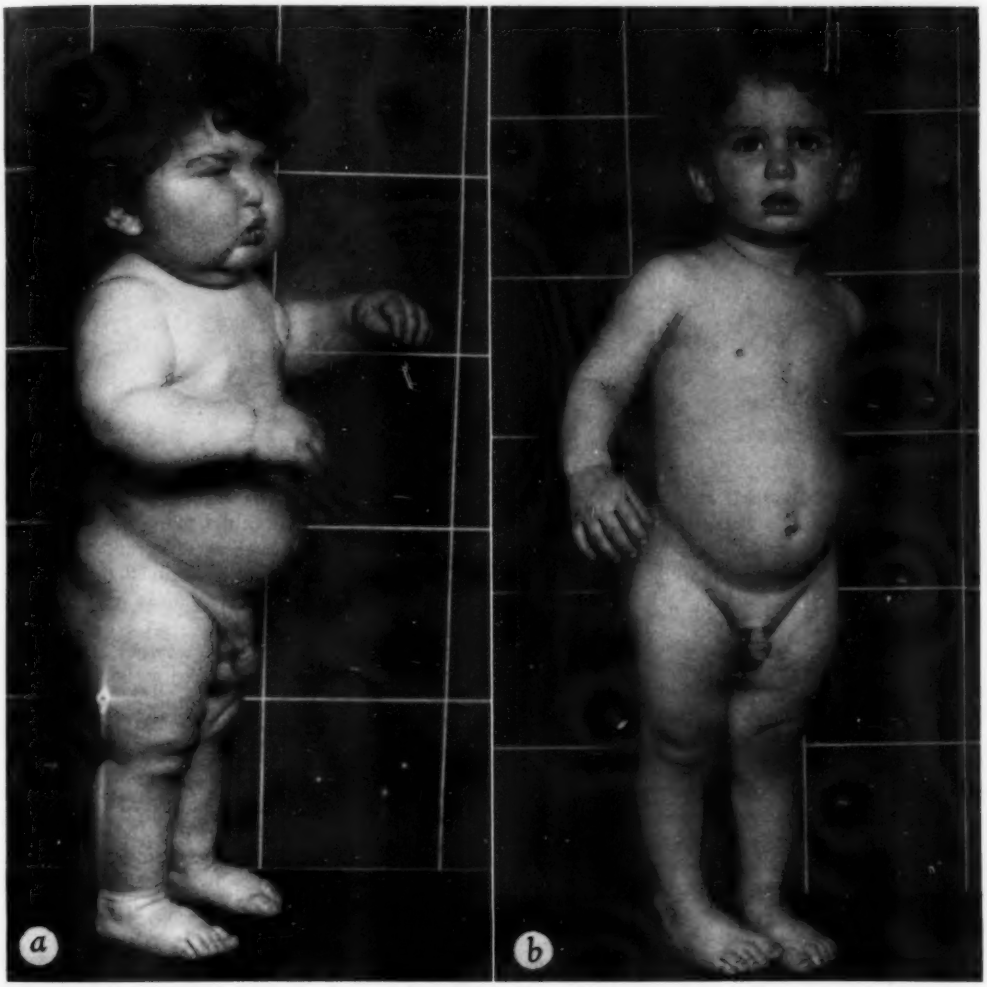

FIGURE 5. Boy aged 15 months. *a.* Before removal of right adrenocortical tumor on May 1, 1942. Dimensions, 6 by 5 by 2.5 cm. low grade cortical adenocarcinoma. Weight, 40 gm. *b.* After removal of lesion.

She was menstruating, and you can see the hirsutism. She had a hyperfunctioning adrenocortical tumor.

Figures 3 and 4 are photographs of another female child who had a malignant adrenocortical tumor, with recurrence of the tumor and re-appearance of symptoms in two years.

(Figure 5): The characteristic fish-mouth type of oral orifice may be seen as well as the hirsuties, the narrowing of the hair line on the forehead, the hirsutism and the acne of the face.

The patient shown in Figures 6 and 7 had a hyperfunctioning tumor of the adrenal cortex. Figures *6a* and *7b* were taken during the time that she had her tumor. Note also the normal appearance after its removal.

Dr. Thompson, this is such a complex subject I am sure you can make some comments which would be appreciated.

DR. THOMPSON: The only comment that I should like to make is that your results with removal of the largest part of the adrenal cortex for Cushing's disease are very interesting. I don't think there is any doubt that Cushing's

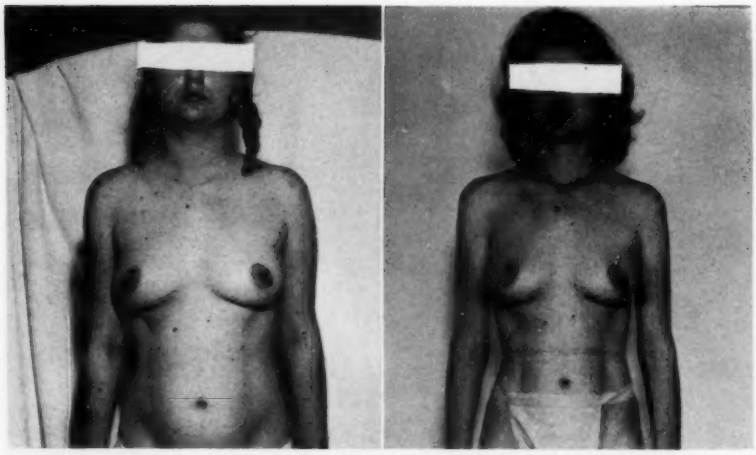

FIGURE 6. Woman aged 24 years. Left adrenocortical tumor removed January 16, 1948. The lesion which measured 3 by 2.5 by 2 cm. was an encapsulated cortical carcinoma of low grade, weighing 10.5 gm. *(left)*. Before operation. *(right)*. After operation.

syndrome may be caused either by a primary adrenal lesion or by stimulation of the adrenal by the pituitary. Wouldn't you agree with that?

DR. WALTERS: Yes, I do. Thank you very much.

PANCREATIC LESIONS

DR. WALTERS: This woman who is 62 years of age has kindly come down here. She has had hypertensive heart disease for quite a while. During the course of her hypertensive heart disease a severe attack of upper abdominal pain developed. Where was that pain?

PATIENT (pointing to epigastrium): Right across here.

DR. WALTERS: Right across the upper part of the abdomen. I have no time to discuss the details of this case, but I will ask her two or three leading questions and then will compare her symptoms with those of the young man who will follow. Did you have any pain in the back?

PATIENT: I don't recall any back pain.

DR. WALTERS: She said she had no pain in the back with the severe pain which she had in the upper part of the abdomen. She had rigidity of the upper part of the abdomen and leukocytosis. She was under Dr. Sloan's and Dr. Guy's care, and after things quieted down a little Dr. Guy drained the gallbladder and her common duct. She had a necrotic, edematous pancreas. That was in March, was it?

PATIENT: March 10.

DR. WALTERS: Since then she has been free of abdominal symptoms relating to her biliary and pancreatic tract. She had had indigestion of the cholecystitis type for a short time prior to her severe attack of abdominal pain, and Dr. Sloan wanted her to get a cholecystogram. She postponed it and then the clinical diagnosis was readily made from the symptoms which I have reported to you.

She well illustrates the fact that in spite of marked hypertension and treatment for it with restriction of activities she could be operated on safely when an acute severe abdominal emergency appeared and she has had a good result.

(To the patient): Thank you.

This man is younger. He had abdominal pain. Where else did you have pain?

PATIENT: I had pain in the stomach and back.

DR. WALTERS: Where was the pain the worst?

PATIENT: The pain was worse, as I remember it, in the back.

DR. WALTERS: He had severe pain in the abdomen and back with digestive disturbances and a palpable abdominal tumor. The resident made a diagnosis of a tumor of the pancreas, which the patient was found to have at operation, but a small amount of tissue removed for microscopic section was reported to be inflammatory. He now has a tumor which can be palpated, and he has a little thickening in his scar which is suggestive of the other type of lesion, the neoplastic one. Why then was inflammatory tissue the report from the biopsy? Because that was the tissue that the pathologist received, and probably the malignant lesion was deeply situated in the tissue.

As the patient continued to have severe pain in the back and abdominal pain a bilateral

FIGURE 7. Same woman as shown in Figure 6. *a*. Before advent of symptoms. *b*. Preoperative view showing acne of face. *c*. Postoperative view six months later.

splanchnicectomy was performed. How are you now? Are you free of pain?

PATIENT: I am free of pain—of that pain.

DR. WALTERS: Thank you very much. You may slip out, if you wish. In other words, he has a fixed large lesion, inoperable, at the tail of his pancreas. He has complete relief of pain by bilateral splanchnicectomy.

I want to say in regard to pancreatic lesions that here also is an organ which all of us can afford to spend a good deal of time studying.

THE tests of abnormal pancreatic function are helpful in making a diagnosis of pancreatitis when they indicate an increased concentration of serum amylase and serum lipase and when this increase is associated with attacks of severe abdominal pain and with abdominal pain and tenderness. A patient, however, may have pancreatitis with all of the clinical signs and symptoms and yet have no elevation of either his serum amylase or his serum lipase. In other words, it is the same old story of the greater value of a clinical history and of the physical findings over the laboratory results if the latter do not conform, and one can apply it anywhere in making differential diagnoses. It is particularly true in obstructive lesions of the biliary tract where there is a question of whether it is an extrahepatic lesion, that is, an obstructive surgical one, or an intrahepatic nonsurgical one. Sometimes it is difficult to make the diagnosis, particularly if there is little, if any, pain. As my colleague Dr. Butt has so frequently said, if the laboratory tests—no matter how accurate they are considered to be—in general do not jibe with your clinical judgment from the history, the physical findings and the course that the patient pursues during your days of observation, stick with your clinical diagnosis and you will be more frequently right than if you rely only on the laboratory tests which relate to hepatic disease.

REFERENCES

1. CAHILL, G. F.: Air injections to demonstrate the adrenals by x-rays. J. Urol. 34:238-243 (September) 1935.
2. WALTERS, WALTMAN and SPRAGUE, R. G.: Hyperfunctioning tumors of the adrenal cortex; study of nine cases. J.A.M.A. 141:653-656 (November 5) 1949.
3. WALTERS, WALTMAN and SPRAGUE, R. G.: Hyperfunctioning tumors of the adrenal cortex with report of eight cases. Ann. Surg. 129:677-701 (May) 1949.
4. POORE, T. N., DOCKERTY, M. B., KENNEDY, R. L. J. and WALTERS, WALTMAN: Abdominal neuroblastoma. Unpublished data.
5. WALTERS, WALTMAN and KEPLER, E. J.: Surgical lesions of the adrenal glands. J.A.M.A. 111:1061-1065 (September 17) 1938.
6. WALTERS, WALTMAN, WILDER, R. M. and KEPLER, E. J.: The suprarenal cortical syndrome with presentation of ten cases. Ann. Surg. 100:670-688 (October) 1934.
7. GREEN, D. M., NELSON, J. N., DODDS, G. A. and SMALLEY, R. E.: Bilateral adrenalectomy in malignant hypertension and diabetes. J.A.M.A. 144:439-443 (October 7) 1950.
8. KEPLER, E. J., SPRAGUE, R. G., MASON, H. L. and POWER, M. H.: The pathologic physiology of adrenal cortical tumors and Cushing's syndrome. In Recent Progress in Hormone Research, the Proceedings of the Laurentian Hormone Conference. New York, Academic Press, Inc., 1948, vol. 2, pp. 345-389.

Diagnostic Clinic

Atresia of the Esophagus With or Without Tracheo-Esophageal Fistula

WILLIS J. POTTS*

NORTHWESTERN UNIVERSITY MEDICAL SCHOOL, CHICAGO

It has been only six years since the first case of congenital tracheo-esophageal fistula and atresia of the esophagus was successfully operated upon—the fistula closed and an end to end anastomosis of the esophagus established—by Cameron Haight. It is a difficult problem and the success of treating it depends upon the early diagnosis.

There are various types of deformities but I am going to discuss only two. The most common type is congenital atresia of the upper end of the esophagus with a fistula between the lower end of the esophagus and the trachea just above the bifurcation. Of 42 cases, 39 have been of this type and only 3 have been cases of atresia of the esophagus with no communication with the trachea.

At postmortem examination the bronchial mucosa is very inflamed because of aspiration of saliva and stomach contents into the lung.

Diagnosis is all-important in this disease which probably occurs once in 2000 to 3000 births. Anyone can make the diagnosis if he thinks of it, but if you have delivered 1500 babies and have not had a case of tracheo-esophageal fistula, you wouldn't be human if you didn't overlook the condition in the 1501st.

If you will bear in mind that the child who breathes poorly after delivery, has excessive mucus in and around the mouth and chokes and has cyanotic spells immediately after birth may have a deformity of the esophagus, you can easily make the diagnosis. Of course, such symptoms are not uncommon in a newborn child. We have seen children with tracheo-esophageal fistulas who have had all sorts of treatment in order to stimulate breathing; they have had atropine, they have had CORAMINE®; one of them had contrast baths—first in warm water and then in cold water—a procedure that ought to make anybody breathe. Imagine coming from a nice, comfortable 99.6° F. temperature into a cold bath. Even such drastic stimulation is not successful because the upper end of the esophagus is choked with fluid which tips into the trachea and causes the child to choke.

If the diagnosis is not made at birth, which, of course, is the optimum time, it is easily made by inserting a catheter; if a catheter cannot be inserted more than 11 cm. from the gum margin, the diagnosis is probably esophageal atresia. As soon as the youngster is fed, the diagnosis becomes obvious; the nurse tries to feed the baby and promptly it regurgitates, so she makes a note on the chart, "Baby fed, baby regurgitated." The doctor comes around, reads the chart and mumbles, "Baby regurgitated. Hmm, most of them do." Go into the room with the nurse and give the baby a little water or formula and you will see that just as soon as the baby swallows, the fluid comes right back up and the baby has a choking spell and coughs. When you see these symptoms, be suspicious of the cause and confirm the diagnosis with the use of some LIPIODOL® (Figure 1).

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Presented at the thirty-fifth (Chicago) annual Assembly of the Interstate Postgraduate Medical Association.

An anteroposterior esophagram taken after injection with a catheter of 2 cc. of warm lipiodol into the esophagus will show that the dilated upper end of the esophagus ends blind. This is the usual type with a fistula between the esophagus and the trachea. There is air in the stomach and in the intestines. The stomach is tremendously dilated. The child breathes, the air goes through the tracheo-esophageal fistula, down the esophagus and into the stomach. So at once you know that this is a case of atresia of the esophagus with a tracheo-esophageal fistula.

Practically all of these children, unfortunately, by the time the diagnosis has been made and they have been admitted to the hospital, have collapse of the right lung with the heart pulled over to the left side. Usually they have some pneumonia.

Never use barium to establish the diagnosis; the following case explains why: A youngster was suspected of having a tracheo-esophageal fistula, and barium was given with a teaspoon—the second mistake. The child, of course, aspirated much of the barium and swallowed a little of it. The child did not have a tracheo-esophageal fistula, as was apparent by the presence of barium in the stomach. The barium which was aspirated into the lungs produced a severe bronchopneumonia. If you give lipiodol with a teaspoon you are apt to get a bronchogram instead of an esophagram. Put it in with a catheter. If lipiodol spills over into the trachea no harm will be done.

As soon as you make the diagnosis, put the baby in an incubator with oxygen, preferably with some humidity. You will have to have a nurse in almost constant attendance. She will have to aspirate the esophagus every half-hour to remove the saliva which is constantly tipping over and being aspirated into the lungs. Aspiration of this thick saliva causes atelectasis by plugging the bronchi. Promptly start administering antibiotics—penicillin and streptomycin. There is a tendency to give these youngsters too much fluid. The average baby needs around 60 to 70 cc. per day. Give these children from 40 to 50 cc. Too much fluid may result in edema of the lungs. Give not more than 10 cc. of physiologic saline solution per pound of body weight—40 to 50 cc. per pound total.

Early operation is in order. A few hours, sometimes a day, can be well spent in preoperative preparation if the infant's condition demands it.

WILLIS J. POTTS

In the old days a gastrostomy was done and nothing else, and attempts were then made to feed the baby. It is an absolutely useless procedure. You sign the baby's death warrant with just a gastrostomy, because the baby will regurgitate the milk up the esophagus and into the trachea and will die of aspiration pneumonia or plain drowning.

A WORD about prognosis. What are you going to tell these parents about the outlook for their baby before the operation is done? In general it is not good. Here is what we have found in 42 patients. The weight is extremely important. Ten of these children weighed less than 5 pounds at birth and less than that when they were brought to the hospital for treatment. Of these, 7 underwent surgery and all died. Four were premature. Nine had other congenital deformities. Three had associated atresia of the rectum. Practically all had pneumonia or atelectasis, or both. The average age on admission was 4.1 days.

You see that you are dealing with a difficult problem—an infant who is too weak to cry and too feeble to cough, but who has to undergo a two hour to three hour operation.

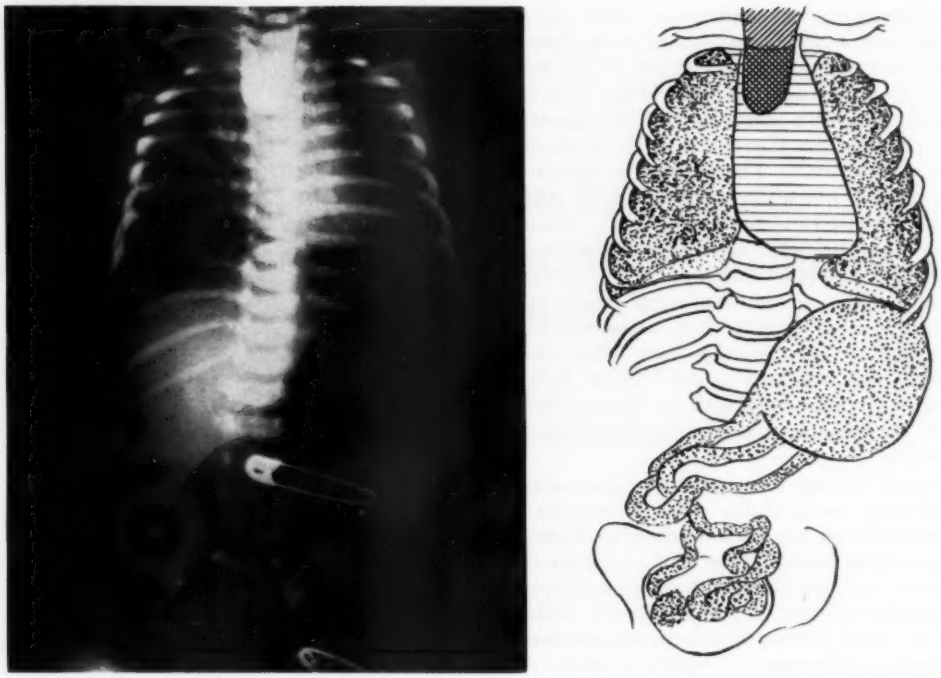


FIGURE 1. This roentgenogram illustrates the common type of atresia of the esophagus with tracheo-esophageal fistula. The upper segment of the esophagus is blind—the lower segment of the esophagus is attached to the tracheobronchial tree as indicated by the presence of air in the gastrointestinal tract.

THE objective of the operation is to close the fistula and establish continuity of the esophagus. The operation is done with the child lying in a prone position. We have tried all sorts of anesthetic agents—cyclopropane, intratracheal anesthesia, pressure anesthesia—and we have come back to ordinary open mask ether with a laryngoscope and intratracheal tubes ready for an emergency.[1]

A parascapular incision is made and, instead of resecting three ribs as we used to do, we take out the third or fourth rib subperiosteally as far forward as possible. This gives adequate exposure. The pleura, as thin as gossamer, is very carefully dissected away from the back so that this is an extrapleural procedure. The pleura should not be opened, because this produces a pneumothorax. The upper end of the esophagus is relatively easily identified; if it is not seen, a catheter inserted in the throat easily identifies it. The lower end of the esophagus practically always enters the trachea at the carina where the bronchi arise from the trachea. It is usually a third to a fifth, but sometimes a tenth, the size of the upper end.

We have modified the procedure from time to time, and we now use the following technic: First, the esophagus is cut off from the trachea. The esophageal stump is transfixed and then closed carefully. The lower freed end of the esophagus is caught with a fine-toothed clamp—the same kind we use to repair a patent ductus arteriosus. It has very fine teeth which will hold the esophagus but will not injure it. The upper blind end is pulled down, a similar clamp is put on and the esophagus is opened. Then, while holding the clamps with the ends of the esophagus apposed, we place the first row of sutures using six zero silk, which is finer even than arterial silk, on a very tiny needle. Two rows of interrupted stitches are put in; first the mucosal layers are brought together, and then the muscular layers are brought together with a similar row of interrupted fine silk stitches. After the anastomosis is completed, the anesthetist expands the lung by fitting a mask over

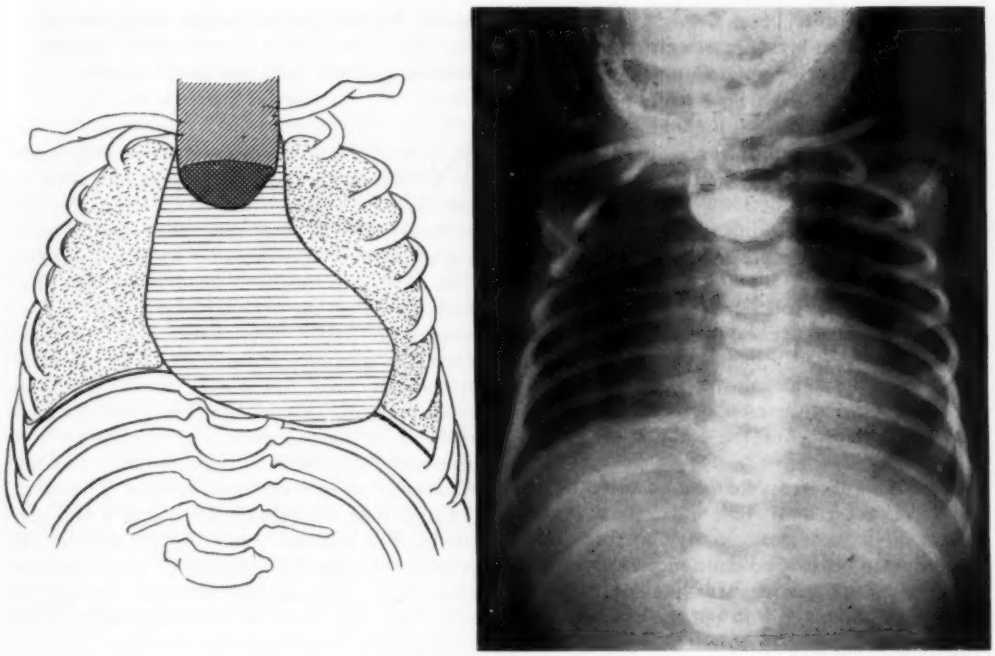


FIGURE 2. This roentgenogram illustrates the less common type of atresia of the esophagus without tracheoesophageal fistula. The upper blind end of the esophagus is filled with lipiodol. The absence of air in the gastrointestinal tract indicates that the lower segment of the esophagus does not communicate with the air passages.

the child's face and making pressure on the anesthetic bag.

We used to make the great mistake of draining these wounds through the wound itself. Air sometimes was sucked in along the drain and produced an extrapleural pneumothorax. The drain is now put in the chest wall through a separate tiny stab wound through the spinal muscles. It is brought down to a point near the anastomosis where it is fixed to the back with a stitch of catgut to keep it from moving against the anastomosis. When the child is returned to his room, constant suction is put on this drain with 10 cm. of water—negative pressure. This suction not only removes any blood or serum and material which might leak from the anastomosis but also removes any extrapleural air which might prevent the lung from reexpanding.

Postoperative care—The child is placed in an oxygen tent. Penicillin and streptomycin are continued. If the infant does not cry, it is stimulated to do so by snapping it on the bottom of its feet. Crying helps them get rid of plugs of mucus in their chests.

We begin feeding on the third or fourth day, giving first a little glucose water and slowly building up a maintenance formula.

We do a gastrostomy only if there is considerable leakage—some of them do leak. We do not like to do a gastrostomy postoperatively to feed these children because it often causes a great deal of trouble. If the child can swallow enough food, we avoid it.

I WANT to present this first patient, now 3 years old, to prove that once in a while these infants get well following surgery. It is important to remember when these children come in—I almost forgot to mention this—to look them over for other deformities. It is very humiliating to find, after beautiful repair of a tracheoesophageal fistula, that you have overlooked, for example, an atresia of the rectum.

We have with us today a little girl who had a

typical tracheo-esophageal fistula. A roentgenogram of the chest was almost normal except for some atelectasis or pneumonia on the right side.

She was frightened a little while ago because she thought she was coming here for another dilatation. This youngster was born July 20, 1947, and was admitted to the hospital seven days later. She had the same trouble that all of these children have—difficulty in breathing—and when attempts were made to feed her, she vomited everything.

This child was operated on and an x-ray taken two weeks later showed the beginning of a stricture. She had a bad leak from the back, but it healed spontaneously. Later, a lipiodol study showed that the esophagus was fairly well obstructed. Because of the leakage, a gastrostomy was done.

This youngster required postoperative dilatations. Whenever a stricture develops, it is important to have a gastrostomy, because retrograde dilatations can be done more safely than dilatations from above. This patient required 12 to 15 dilatations to iron out the esophagus to proper size. Then, as so often happens, the child was not brought back for about six or eight months because she seemed all right. She was admitted then as an emergency. She was old enough to swallow food and, as children do when they are hungry, she had swallowed a piece of meat without chewing it properly and it had lodged at the old stricture. Dr. Holinger removed this chunk of meat and later dilated the esophagus once more. Since then she has been well. This child has had to have more dilatations than any of our patients—15 in all—and it is no wonder she is a little frightened.

Thank you very much for coming.

I can't tell you the problem she was during those three weeks in the hospital—formula running out of her back, dehydration, pneumonia, etc. When you see the little girl as she is today, the effort seems worth while.

A somewhat similar case—a doctor's child who was flown in from Iowa—presented the typical x-ray picture. The upper end of the esophagus was short, coming down only to the second thoracic vertebra. We were very fearful that we would not be able to get the ends together, but we did and after two weeks she had a fairly normal looking esophagus. When the ends of her esophagus were sewed together they were under so much tension that as one pulled across it, a twanging sound was heard. Maybe that is a slight exaggeration, but the ends were under a tremendous amount of tension and still held and grew together.

Now we have the other group, which is represented by the cute little dolly sitting on the chair here. She presented the same sort of a deformity in the esophagus, with one outstanding difference—there was no air in the stomach. The answer to that, of course, is that the child had atresia of the esophagus *without* tracheo-esophageal fistula. Consequently air could not enter the gastrointestinal tract. The esophagus has a very small lower end in all these cases, often no larger than a slate pencil and not more than an inch or so above the diaphragm. It is absolutely impossible in most instances to bring these ends of the esophagus together (Figure 2).

Come here, sweetheart. Of course I am terribly fond of this child, and I might say that the practice of pediatric surgery is wonderful because you can hold any of your patients on your lap and never be misunderstood. (This little girl was 3 years old on December 10, 1950.) She was brought to the Children's Memorial Hospital in December 1947 weighing 5 pounds 3 ounces. She had congenital atresia of the esophagus without tracheo-esophageal fistula. The incision was made in the back and we attempted an anastomosis but it was absolutely impossible to bring the ends of the esophagus together, even by pulling them as hard as we dared.

The chest wall was closed. We did a gastrostomy after a couple of days. That was perfectly safe because the lower end of the esophagus was atretic. We later exteriorized the upper end of the esophagus at the neck. We let this youngster go like this for a year. Then we wondered what to do. Obviously a child should not go through life with a gastrostomy. It is not fair to an unsuspecting child who can't talk back to condemn her to a permanent gastrostomy.

About this time we heard about an operation which had been done by Rienhoff of Baltimore and which seemed very feasible. We opened the abdomen, freed the stomach, removed the lower end of the esophagus, closed the gastrostomy, cut the various vessels where necessary and made a pouch underneath the skin of the chest. Then we pushed the stomach up under the skin anterior to the sternum and anastomosed the fundus of the stomach to the upper

end of the esophagus with two rows of interrupted silk sutures.[2]

The operation was relatively simple and the child made an uneventful recovery. However, her stomach enlarged tremendously beneath the skin and it was very unsightly. No child had survived this procedure for a long period of time, so nobody knew just what the ultimate outcome was going to be. That stomach was truly enormous and you could see a peristaltic wave going down although the vagi were not intact. When she had a good meal she just put her chin in her fundus and was quite happy. However, no girl can go through life with an appendage like that on her chest. So what were we to do? We could do one of two things: (1) cut the anastomosis, bring the stomach through the diaphragm and then re-anastomose it in the chest, or (2) perform an operation which we had tried post mortem a number of times and which looked feasible. Following the latter course, we separated the stomach from its attachment to the skin and cut all the ribs on the left of the sternum. We had to take out the middle half of the clavicle and the middle half of the first rib so that there would be room for the esophagus to go over the bump. Then we swung the stomach around behind the lung and the heart until it lay in the posterior gutter of the chest and fixed it there with a few sutures. The diaphragmatic opening was closed about the stomach. The ribs were apposed with single sutures and the wound was closed.

The child survived this operation very well, but she was a little difficult to handle and no wonder. By this time she had been in the hospital 120 days, had had 20 million units of penicillin and streptomycin representing some 600 injections and had had 51 intravenous administrations of fluid, plasma, blood, etc. The look of defiance on her face in a photograph taken two weeks after operation was justified.

She had some trouble breathing immediately after the operation; this was due most likely to fright because as soon as her mother came to the hospital to care for her she did all right. For a long time she objected strenuously to the approach of anybody resembling a doctor, but now she has made friends again. All has been forgiven or forgotten. Her stomach is in her chest, she eats normally, plays hard and is—although rather tiny—a healthy, attractive child.

Thanks very much for coming.

I MIGHT say in summary that there is no operation in the surgical textbooks which is as difficult technically as the repair of a tracheo-esophageal fistula. You look at some of these puny infants and say there isn't a chance, and yet some of them do survive.

Here is what has happened to the mortality rate in this condition. Some of our 42 patients had deformities of one kind or another that needed to have care first, so that finally we had 32 on whom end to end anastomoses of the esophagus could be done. Fifteen of these children have survived. In the early days the mortality rate was 70 per cent. During the past year it has dropped to 27 per cent. Eight of the last 11 patients operated on have survived, due, we believe, to improved technic and better preoperative and postoperative care.

I am sorry that time does not permit a discussion of what to do with the child who has atresia of the esophagus without a fistula. If there is a fistula, do an end to end anastomosis if at all possible. This operation will give the child a good esophagus. If the child does not have a fistula, the ends of the esophagus are apt to be so widely separated that you won't be able to bring them together. Some kind of an anastomosis will have to be done, because the child can't go through life with a gastrostomy. We prefer bringing the jejunum up through the chest or behind the sternum and anastomosing it to the upper end of the esophagus. Any structure such as the stomach or bowel under the skin is apt to be unsightly.

Remember that the newborn child who breathes poorly at birth, has much mucus, has attacks of cyanosis and immediately regurgitates any fluid given probably has atresia of the esophagus with a tracheo-esophageal fistula. Early operative reconstruction of the esophagus is the treatment of choice.

REFERENCES

1. POTTS, W. J.: Congenital atresia of the esophagus with tracheo-esophageal fistula. J. Thoracic Surg. 20:671, 1950.
2. POTTS, W. J.: Congenital atresia of the esophagus; antethoracic placement of the stomach followed by intrathoracic transplantation. J. Thoracic Surg. 20:701, 1950.

SCIENTIFIC EXHIBIT

Meckel's Diverticulum

THOMAS A. SHALLOW, SHERMAN A. EGER
AND FREDERICK B. WAGNER, JR.*

JEFFERSON MEDICAL COLLEGE AND HOSPITAL, PHILADELPHIA

Grave complications frequently associated with Meckel's diverticulum transform its role from a mere surgical curiosity to one of importance in both acute abdominal emergencies and elective laparotomies.

The purpose of this exhibit is to illustrate
1. The varying clinical manifestations.
2. The difficulties in diagnosis.
3. The problems in treatment.

} In a series of 75 Cases

HISTORICAL DATA

1672 Lavater first mentioned its existence.

1701 Ruysch published the first illustration.

1742 Littre reported its presence in a hernia.

1812 Meckel first accurately described the lesion, included its embryologic significance and stressed its clinical importance.

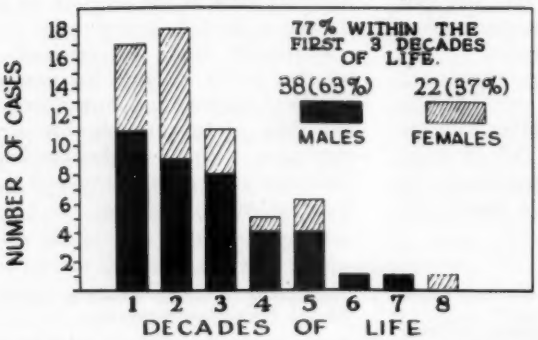
1861 Zenker found aberrant pancreatic tissue in its wall.

1904 Salzer found gastric mucosa in its wall.

1925 Schaetz associated Salzer's find with ulceration and bleeding.

INCIDENCE

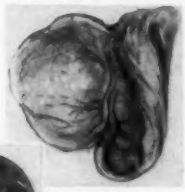
- Found in approximately 2% of all individuals.
- Is 20 times as common as cleft palate and harelip.
- Is more common in males. (63% in this series.)
- May occur in the colored race. (1 in this series.)
- Rarely found in more than one member of the family.
- Average age at discovery was 25 years in this series.
- Complications were present in 25% of the series.

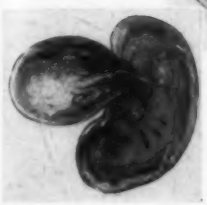


DISTRIBUTION OF 60 SURGICAL CASES ACCORDING TO AGE GROUP AND SEX

*From the Samuel D. Gross Division of Surgery, Jefferson Medical College and Hospital, Philadelphia, Pennsylvania. This exhibit received an honorable mention citation at the New Jersey State Medical Convention in May, 1951.

.....NORMAL EMBRYOLOGY....





Early in fetal life the intestine communicates with the yolk sac for nourishment.

By the fourth week ..... the opening gradually narrows to form a tubular structure known as the vitelline duct.

At the 7mm. stage the mid-gut normally closes off completely by atrophy of the vitelline duct to form a fibrous cord.

The fibrous cord between umbilicus and bowel is subsequently absorbed.

....ABNORMAL EMBRYOLOGY....

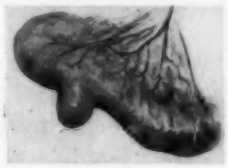
(ETIOLOGY)

Failure of all or part of the vitelline duct to become obliterated accounts for the various forms of this lesion.

Fibrous cord persists and extends from diverticulum to umbilicus, to adjacent bowel or to mesentery.

Vitelline duct remains patent throughout.

Persistence of the proximal portion of the vitelline duct results in formation of Meckel's diverticulum.



Aberrant pancreatic tissue may form in the wall of Meckel's diverticulum.

Gastric, duodenal or colonic mucosa may occasionally form part or all of the mucosal lining of the diverticulum.

GROSS PATHOLOGY

Location:

15 to 100 cm. (Average 80 cm.) proximal to the ileocecal valve.

Site of Origin from Ileum:

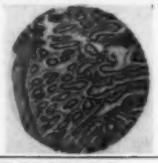
From antimesenteric side.

Size:

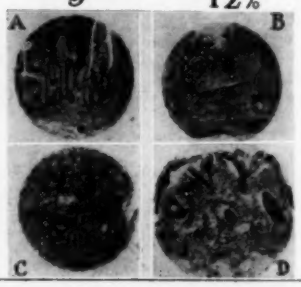
1 to 8 cm. long. Diameter slightly less than that of ileum.

MICROSCOPIC PATHOLOGY

The wall of the diverticulum was the same as ileum in

58 cases  ...88%

MUCOSAL LINING		
TYPE	CASES	PERCENT
ILEAL ONLY	66	88%
ABERRANT	9	12%
A Gastric and Ileal	4	
Gastric and Ileal with ectopic pancreatic tissue	1	
B Duodenal and Ileal with ectopic pancreatic tissue	1	
C Ileal, with ectopic pancreatic tissue	2	
D Colonic and Ileal	1	



ASSOCIATED ABNORMALITIES

(18 cases or 30%)

One case of each:
- Harelip
- Esophageal atresia
- Patent foramen ovale
- Cyst of ileum
- Dermoid cyst of ovary
- Endometriosis
- Malformation broad ligament
- Diverticulum of urinary bladder

Two cases of each:
- Congenital peritoneal bands
- Accessory spleen
- Malrotation of colon

Four cases:
- Hernial defects

....COMPLICATIONS....

Meckel's diverticulum is subject to a wide variety of serious pathologic complications. Knowledge of these is essential for the understanding of the varied and confusing clinical pictures which the lesion may present.

1
INFLAMMATION

(Without perforation)

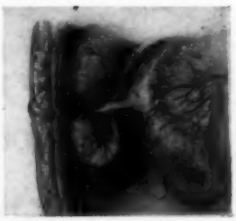
(With perforation.)

2
ULCERATION

With or without hemorrhage.

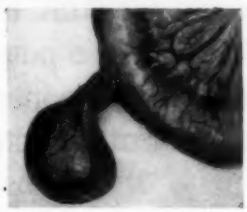
3
INTESTINAL OBSTRUCTION

From unabsorbed band.



4
INTUSSUSCEPTION

5
TORSION



6
PRESENCE IN A HERNIAL SAC

(Littre's Hernia)

7
TUMORS

Benign and malignant.

NONE FOUND IN THIS SERIES

8
FISTULA To Umbilicus.

DIAGNOSIS

In practically all cases, the diagnosis of Meckel's diverticulum can be made with certainty only at operation.

Symptoms and Signs:

The diverticulum causes no symptoms in the majority of cases (72%), and is usually found at laparotomy for some other condition.

When symptoms occur, the clinical picture varies with the type of complication present.

1. **Inflammation** simulates appendicitis and its complications.
2. **Hemorrhage** simulates that from other intestinal sites.
3. **Intestinal obstruction** from intussusception, torsion or bands.
   Littre's hernia or neoplasm give no clue to the diverticular origin.
4. **Fecal fistula** at umbilicus strongly suggests patent vitelline duct.

Laboratory Findings

1. **Blood Count:** Varies with inflammation and hemorrhage.
2. **X-Ray:** Is of little value in demonstrating a Meckel's diverticulum. However, the injection of a radiopaque medium into an umbilical fistula, differentiates a patent vitelline duct communicating with the intestine from a patent urachus communicating with the urinary bladder.

At Operation:

Search for Meckel's diverticulum at laparotomy should be made in all cases in which

1. The anticipated lesion is not found.
2. Intestinal bleeding has been a symptom, particularly in children.

....TREATMENT....

SURGICAL EXCISION IS THE TREATMENT OF MECKEL'S DIVERTICULUM.

Indications:

1. When the diverticulum produces symptoms.
2. When the diverticulum is found incidentally at laparotomy for some other condition.
   (Except as listed under contraindications.)

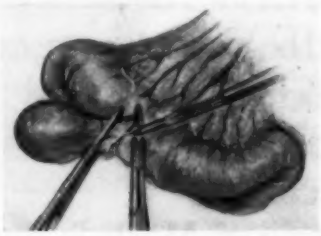
Contraindications:

When found incidentally at laparotomy....

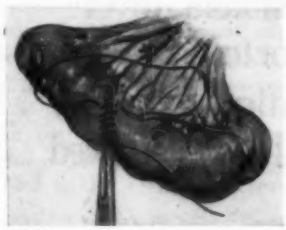
1. In association with severe, acute inflammations of other structures.
2. In association with acute, intestinal obstruction, not of diverticular origin.
3. In poor risk patients.
4. In patients with metastatic malignancy.

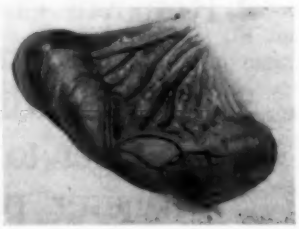
Technic:

1. Excision of diverticulum with cautery between clamps placed obliquely at base.



2. Ileum repaired with continuous double layer of catgut suture, reinforced with interrupted black silk.





MECKEL'S DIVERTICULECTOMY~60 CASES★

OPERATIVE FINDINGS	RECOVERY	DEATH
Inflammation alone:		
Without perforation	5	0
With perforation	4	0
Inflammation with obstruction from band	1	0
Inflammation with intussusception	1	1 (a)
Inflammation with volvulus	1	0
Obstruction from band	2	0
Intussusception	0	1 (b)
Ulceration	1	0
Umbilical fistula	1	1 (c)
Found incidentally	41	0
Total	57 (95%)	3 (5%)

★Not included in this table are:
4 cases (Incidental diverticulectomy not performed)
11 cases (Found incidentally at autopsy)

ANALYSIS OF DEATHS

(a) White male; 11 mos. old; died from shock (1936) following reduction of intussusception, diverticulectomy and ileostomy (ectopic pancreatic tissue in wall).

(b) White female; 3 yrs. old; died of intestinal obstruction (1936) following reduction of intussusception and diverticulectomy.

(c) White female; 7 mos. old; died of peritonitis (1937) following excision of fistula; also had patent foramen ovale of heart.

CONCLUSIONS

1. Incidental search for Meckel's diverticulum at laparotomy should be just as routine as for the appendix.
2. Signs of appendicitis, associated with intestinal bleeding, especially in a child, strongly suggest Meckel's diverticulitis.
3. The complications of Meckel's diverticulum are serious and carry a high mortality.
   (15.8 % in this series.)
4. Removal of an uncomplicated Meckel's diverticulum carries practically no mortality.
5. Meckel's diverticulum is a potential source of danger to the patient and should be removed whenever possible.

GENERAL PRACTICE *Review*

To provide the general practitioner, as well as the specialist, with concise, readily available information on the latest, proved methods of treatment of conditions commonly encountered in an average practice, POSTGRADUATE MEDICINE *offers this department to its readers. It is not, of course, intended to present these discussions as the only acceptable therapeutic procedures to be used, but rather to offer simple regimens and recommendations based on the extensive experience of the physicians who prepared these summaries.*

The Medical Treatment of Ulcerative Colitis

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BARGEN

ULCERATIVE colitis presents itself to the physician in many forms. When a physician uses the term "chronic ulcerative colitis" he is speaking of a series of serious human maladies. A patient who has ulcerative colitis may be ill for a long time, and he may need a physician's constant care and observation for a very long time. We should think of the various forms of chronic ulcerative colitis as we do of other chronic destructive infections. Quick healing and rapid recovery are rare, even in milder ulcerative colitis. Slow progressive improvement and ultimate recovery are very common, even when the disease is most severe. Since all forms of inflammation of the large intestine could be considered in the nature of a colitis, it would seem well to limit the present discussion to three common forms of ulcerative colitis.

First is that form of ulcerative colitis which has its inception at the anal canal and lower part of the rectum and which spreads relentlessly orad, and is commonly known as "thrombo-ulcerative," or as the "streptococcic" form of the disease.

Second is a form of ulcerative colitis which may start in any segment of the large intestine and spread in both directions. It may be, and more commonly is, in the nature of disseminated ulcerative disease, or a diffuse form of ulceration may be present in segments of the large intestine.

Third is a segmental or regional form of ulcerative colitis involving segments of the colon above the region of the rectosigmoid.

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THROMBO-ULCERATIVE COLITIS

The first form of ulcerative colitis is a diffuse disease, the lesions of which begin at the anal canal. Diffuseness of involvement, no matter how much colon is involved, is characteristic and pathognomonic of the disease. In the second form, the dissemination of the ulceration is characteristic. In the third form, ulceration of a segment of colon above the rectosigmoid and involvement by advanced disease are common.

Theories of Inception—Various theories of the inception of these infections have been promulgated. Most of these apply more directly to the first form of the disease, but can be applied to the other two as well.

Theory of infection—Through the years many bacteria have been regarded as possible causes, or as at least agents of inception, of the lesions of the thrombo-ulcerative form of colitis. The most convincing evidence of the bacterial relationship in this condition concerns itself with a diplostreptococcus which is commonly found in the initial lesions of the first forms of this disease. Although other bacteria, such as *Bacterium necrophorum* and the common intestinal organisms, may play a role as supporting etiologic agents, this diplostreptococcus is important in the initial inception of the lesions of this disease.

Enzyme theory—Although the disease may be primarily of infectious origin, such enzymes as lysozyme also may have a bearing on the early progression of the disease. At least there is some evidence that the presence of this enzyme in excess may be a factor in the development of some of the ulceration. This enzyme is present in excessive amounts in the gastrointestinal secretions under stimulation by inflammation and irritation. It is possible that an excess of lysozyme in the present of inflammation and irritation might result in some surface ulceration.

Metabolic factor—There is evidence of impairment of adrenal function in patients who have ulcerative colitis, such as changes in the circulating eosinophils, low quantities of 17-ketosteroids and corticosteroids in the urine, and other evidence of severe stress. These factors, again, are probably secondary rather than primary causative factors in the severely diseased patient, but they need consideration in any observations as to the cause and progression of this disease.

Psychosomatic relationships—More recently some physicians have laid greater stress than in the past on the psychosomatic relationships in a variety of inflammatory diseases, and so ulcerative colitis has received its share of attention from this particular viewpoint. The intestinal tract is susceptible to the effects of disturbances of the psyche. Emotional and nervous stimulations are inclined to increase intestinal activity. Whether or not the infectious process is more likely to be initiated during periods of emotional stress and strain it is impossible to say, but it seems probable that once the disease process has been initiated, psychic disturbances easily may aggravate symptoms already present. The very nature of the disease process is one that makes it particularly susceptible to the effects of psychic insults. Yet, although the emotional phase of human activity probably is important in the activity, progression and exacerbation of this disease, it probably does not have an important immediate causative effect.

Need for Analytic Evaluation—A thorough analysis of all the foregoing factors, their importance in various phases of the inception and development of ulcerative colitis and their relationship to the disease in its various stages of development, must be studied in every instance of colitis. Even more important is the definition of each particular instance of colitis from the standpoint of what its cause is believed to be. The vast majority of the patients who have ulcerative colitis of either of the first two types described represent essentially medical problems. There are, however, some complications such as polyposis, stricture, perianal abscess, perforation and the occasional secondary neoplasm which likewise present surgical problems. Then, too, there is the so-called intractable ulcerative colitis which eventually may become a surgical problem.

Treatment—Nearly all the patients present themselves initially as medical problems, but in some of them the complications mentioned may develop later and thus make the situation one which calls for surgical treatment. However, with judicious and painstaking medical care not more than 5 to 10 per cent of these patients should become surgical problems. Medical treatment of these patients readily divides itself into several phases including rest and restful relaxation, suitable diet, tender nursing care, transfusion of blood, maintenance of fluid balance, adequate maintenance of vitamins and use of a variety of drugs and hormones.

Which one of these factors will be most important will depend upon the stage and activity of the disease at the time the patient is encountered. The patients readily can be divided into those who have the insidious form and those who have the severe or fulminating form of the disease. Symptoms of patients who have the insidious form usually are mild and only

the distal segments of the large intestine are involved. In the severe form, the entire large intestine may be involved, but depletion of the body may not be too severe.

Patients who have the fulminating form of the disease are extremely ill. Probably no other infection known causes a greater general body depletion than a prolonged attack of fulminating ulcerative colitis. How much rest will be needed will depend upon the stage of the disease. In the insidious phase of ulcerative colitis, avoidance of overdoing and adequate hours of sleep, say 12 hours in bed at night and several hours' rest during the middle of the day, may be quite sufficient, but in the more severe and fulminating forms, absolute rest in bed is essential. If improvement comes, restful relaxation and freedom from nervous tension become important parts of the program of therapy.

Feeding—The feeding of these patients can present a very difficult problem. Often the diet has been much too greatly restricted with the erroneous assumption that, because of the diarrhea, the intake of food should be limited. Actually, however, since the disease is of a chronic nature, limitation of food for any length of time ultimately will be detrimental. Sometimes complete anorexia occurs as the disease continues. The problem then may be, first, one of creating an appetite and, second, one of giving foods which are readily digestible and which leave a minimum of residue in the large intestine.

In many instances of the severe and fulminating form of ulcerative colitis, it is well to give the digestive tract a rest by omitting all food by mouth and feeding the patient parenterally; however, this method of feeding should be abandoned at the earliest possible time. When the patient can tolerate feeding, adequate amounts of proteins and carbohydrates should be given so that the diet will include well over 3000 calories daily, of which 145 calories or more may well be protein. Iced beverages, condiments and other stimulants should be avoided, and while the diet may be based on broad general principles, it must be adapted to the individual. In some patients who have advanced ulcerative colitis there is a great depletion of the essential vitamins; hence, attention to these—including particularly A, B and C—is of great importance. The use of extra amounts of potent B complexes often is very helpful.

Nursing care—The importance of gentle nursing care during the severe and fulminating phase of the disease cannot be overemphasized, for often a kind nurse who will attend to the many details which arise will mean the difference between satisfactory progress and intractableness of the disease. These patients frequently are seized with great straining at stool and the desire to evacuate the bowels much too often. Gentle persuasion, mild sedatives, hot abdominal stupes and other soothing measures will be helpful.

Transfusion of blood—There is probably no other chronic disease in which so much blood is lost over a long time as in ulcerative colitis; hence, blood and often blood substitutes should be administered. It is not uncommon for a patient who has a severe and fulminating form of ulcerative colitis to require blood to be transfused as many as 12 to 20 times during the severe phase of the disease and during his convalescence in the hospital. It is also to be noted that reactions from transfused blood are more common in this group of patients than in any other group of sick people. For this reason particular attention should be given to grouping, the Rh factor, fasting of the blood donor, preadministration of sedatives and all other measures tending to reduce reactions.

Use of fluids—The parenteral administration of other fluids often becomes necessary. The solutions used are (1) isotonic solution of sodium chloride (9 gm. of sodium chloride per liter of water), (2) modified Ringer's solution consisting of 9 gm. of sodium chloride, 0.24 gm. of calcium chloride, 0.42 gm. of potassium chloride, 0.20 gm. of sodium bicarbonate and 1000 cc. of triple-distilled water and (3) Hartman's solution, consisting of 4.8 gm. of sodium lactate, 12 gm. of sodium chloride, 0.8 gm. of potassium chloride and 0.4 gm. of calcium chloride in 2 liters of solution. The main constituent of all of these solutions is sodium chloride in a concentration which is isotonic or slightly hypotonic when compared with the concentration in the blood. The last two solutions contain other ions which are helpful, but which perhaps are of secondary importance.

Two other solutions used for parenteral administration are (4) 5 or 10 per cent solution of glucose in isotonic solution of sodium chloride.

The indications for the parenteral administration of fluids are (1) dehydration, (2) need for maintenance of water balance, mineral balance and nutrition, (3) presence of acidosis and (4) presence of alkalosis.

In this connection it is particularly important to watch for potassium depletion, for, if it occurs, correction of it may mean the difference between success and failure of an otherwise well planned program.

Fluid requirements for 24 hours are as follows: For the patient who has not had an abnormal loss of fluid: 2 to 3 liters a day in order to get an adequate urinary output of 1200 to 1500 cc. a day and to replace fluid lost in sweating (up to 3 liters may be necessary when loss by sweating is great, as in hot weather, in the presence of high fever, etc.).

For the patient who has had abnormal losses of fluid (vomiting, intubation, severe diarrhea and so forth), the basal requirements of the previous paragraph should be provided plus sufficient fluid to replace the abnormal loss, volume for volume.

Use of drugs—A variety of drugs have been used in the treatment of ulcerative colitis, not only because of the severe nature of these diseases but also because of the constant hope of quick response to some so-called miracle medicine. The advent of sulfonamide drugs raised the hope that patients who had ulcerative colitis might receive prompt relief by the administration of these new therapeutic agents. In many instances this hope was realized. It soon became apparent, however, that drugs useful in the treatment of the various forms of ulcerative colitis are limited not only in number but also in suitability of application. Among those drugs which to date have been found useful because of their relative lack of toxicity and because of their therapeutic effectiveness are azosulfamide (NEOPRONTOSIL®), azopyrin, SULFATHALIDINE®, and various antibiotic agents, such as penicillin, aureomycin and terramycin. Other drugs are constantly receiving therapeutic trial as they become available for experimental purposes.

Regardless of which sulfonamide drug is used, it has been found best to give it in courses. It is administered for two weeks, then the patient rests a week and then administration is continued for a similar period. In this way 60 to 90 gr. (4 to 6 gm.) of azosulfamide can be given in divided doses each 24 hour period to the average adult person. For children the dose should be correspondingly smaller. If sulfathalidine is used, it may be given in doses of from 120 to 140 gr. (8 to 10 gm.) in a 24 hour period. Although the toxicity of both these drugs is very low, reactions to toxicity have been known to occur. When azosulfamide particularly is used, it is important to have the hemoglobin content, erythrocyte count and leukocyte count checked frequently, since anemia is likely to occur without other symptoms of toxicity while the drug is being administered.

Sulfathiazole is well tolerated in doses of 45 to 75 gr. (3 to 5 gm.) daily, but in the use of the drug even more careful observation for toxic effects must be made.

Similarities between the patient acutely ill with ulcerative colitis and the patient ill with rheumatic fever have long been observed. It is because of these similarities that the various salicylates have been given a therapeutic trial. For this purpose various investigators have tried to prepare combinations of sulfonamides and salicylate drugs. To this end, salazopyrin (azopyrin in the United States) has been prepared. This drug originally was prepared by Pharmacia of Stockholm, but is now prepared and distributed in the United States. Our experiences with this drug have been very gratifying. We began its use in those patients who had the complications of arthritis or pyodermic lesions, and since the response in these was satisfactory, the use of the drug was extended. It is at this time the preferred drug in the treatment of severe ulcerative colitis. It is given in doses of 1 to 1.5 gm. every three hours, preferably in courses of, say, two weeks on and a week off.

In some cases of acute fulminating ulcerative colitis, other drugs such as sulfadiazine given in amounts to result in the concentration of 12 to 15 mg. of the drug per 100 cc. of blood sometimes will yield striking relief.

Among the more helpful antibiotic agents have been penicillin and aureomycin, given particularly to the severely ill patient. The patient should receive at least 500,000 to 1,000,000 units of penicillin daily. Aureomycin or terramycin is particularly suitable when the patient is able to take things by mouth. A dose of 750 mg. every four hours has been given. If the patient is too ill to take food or drink by mouth, aureomycin also may be given intravenously. There are other antibiotic agents on the horizon which offer the hope of being at least as satisfactory as, or possibly even more so than, these two agents have been found to be.

Inasmuch as this disease frequently is associated with great bodily depletion, the hormones such as ACTH and cortisone have promise of

being helpful in a supportive manner. When there is considerable disturbance of circulating eosinophils and a marked reduction in the 17-ketosteroids in the urine and other signs of bodily depletion, use of these hormones has been helpful. They should be administered very cautiously and only under careful supervision. A satisfactory dose as yet has not been established, although many patients have received the hormones. Possibly 40 to 80 mg. a day of, say, ACTH would be a suitable dose, but the amount varies, so that it is difficult to set down an acceptable dose. Furthermore, experience with these hormones thus far has not been extensive and when one of them is given as the sole therapeutic agent it has had little effect upon the progress of the disease. Testosterone as an aid to protein metabolism also has been of help to some patients with bodily depletion. Many other supportive measures are brought into play in the control of this devastating infection.

Comment—This entire program and the advisability of use of one of these medications will depend upon the severity of the patient's illness and the damage the disease has done to his bodily economy. The psychosomatic approach to the patient who has ulcerative colitis is important. In his treatment the internist must include methods of combating the patient's anxiety and nervous tension. There is probably no other group of patients, by and large, who need more encouragement and urging to follow a well ordered program than do the patients who have ulcerative colitis. The old saying that "disease above the diaphragm makes for optimism and below the diaphragm for pessimism" is well illustrated in the average patient who has ulcerative colitis.

In about 20 per cent of the patients the disease involves only the distal segments of the large intestine, and most of these patients, if persuaded to follow a well ordered program and if they continue to take their medications wisely, will recover. Once they recover, the condition may be kept under control if the patient is able to avoid infections of the upper part of the respiratory tract and to avoid overdoing in every way. Ulcerative colitis seems to be a disease which demands that the patient live moderately once the disease has been brought under control. It is not always true that improvement is proportional to the extent of intestinal involvement although usually patients who have milder ulcerative colitis recover and those who have more advanced ulcerative colitis have a more difficult time. It can be said, however, that usually when the very sick patients recover they remain well, and that when persistent medical care is employed, most severely ill patients will recover. It is the rare exception for any of them to need a surgical operation. Occasionally one who suffers a massive uncontrollable intestinal hemorrhage or localized perforation may need surgical attention, but these instances are few, and the majority of the patients will gradually and progressively improve.

DISSEMINATED ULCERATIVE DISEASE

Much of what has been said about thromboulcerative colitis also applies to the second group of patients mentioned, namely, patients with irregularly disseminated involvement of the large intestine. No important bacteria or other organisms have been recovered from these patients, and the general problem of therapy has been correspondingly more difficult. The general supportive program and the drugs referred to previously are commonly used in this type of colitis. The response at times is not so satisfactory, and as a rule, more of these patients require surgical treatment than do those of the first group; however, most of these patients respond satisfactorily to the program outlined for the patient who has diffuse colitis.

SEGMENTAL OR REGIONAL ULCERATIVE COLITIS

The patient who has the segmental type of involvement and involvement above the reach of the proctosigmoidoscope also should receive adequate trial of a medical regimen, but if progress is not satisfactory within a reasonable period, and during the stage in which the disease is fairly quiescent, surgical resection of the diseased segment of bowel usually can be undertaken with a satisfactory result. Fortunately in these cases establishment of an intestinal stoma is not necessary. This factor in itself has tended toward the advising of earlier surgical treatment. Generally, the diseased segment is removed and an end to end anastomosis restores intestinal continuity. However, many of these patients also have responded in a satisfactory manner to a general supportive program.

The Local Treatment of Dog Bites

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VINNARD

A STUDY of the various methods used in the local treatment of dog bites quickly reveals some surprising facts. Perhaps one of the most surprising is the great need that exists for investigation, clarification and an attempt at standardization of the local treatment of dog bites. It should be understood that while the term, "dog bite," is used throughout this article, the same situation and treatment apply to any animal bite, inasmuch as most species of animals have been proved capable of transmitting the rabies virus.[1,2]

The old concepts of destroying bacteria in wounds by the use of caustics and strong antiseptics have long been abandoned. Should their use be encountered in the routine treatment of soft tissue wounds, it would quickly be condemned by the entire medical profession. The sound fundamental surgical principles of soap and water cleansing, mechanical debridement, and primary skin closure, if indicated—with or without the use of mild skin antiseptics—are and for years have been universally accepted and satisfactorily practiced in the local care of soft tissue wounds. When carefully carried out, the effectiveness of this routine in ridding wounds of the effects of pathogenic bacteria has been so universally accepted as to require no further elaboration.

Thus it is an uncomplimentary reflection on medical thinking and progress to find that approximately one third of the best teaching hospitals in the United States, with probably a higher percentage of lesser hospitals and private doctors' offices, are treating dog bites with local applications of caustic substances, most commonly fuming nitric acid. Phenol, sulfuric acid, hydrochloric acid, silver nitrate, FORMALIN®, iodine and the actual cautery are other caustic agents in routine use on dog bite wounds in various sections of the country.

RESULTS OF SURVEY

In an attempt to obtain a nationwide perspective of this problem questionnaires were sent to 100 chiefs of surgery at hospitals approved for resident surgery training. Automatically included were the large nationally known charity institutions and the remaining hospitals were chosen on a numerical basis, selecting every tenth one as listed in the educational number of the *J.A.M.A.*

The questionnaires consisted of four questions:

1. What is the routine or most commonly used local treatment of dog bites in the emergency room of your hospital?

2. What is the recommendation of your local public health department as to the local treatment of dog bites?

3. Is there a law in your state requiring nitric acid cauterization of dog bites?

4. *Remarks*—(A statement as to your personal recommendation for the local treatment of dog bites would also be appreciated.)

Question number 3 was included because frequently one hears the statement among doctors that it is required by law to cauterize dog bites.

Of the 100 questionnaires sent out, replies were received from 51 hospitals in 38 cities of 23 states. Of the replies received, 33 gave soap and water cleansing as the routine or usual treatment. Seventeen replies indicated the routine use of caustics, which included 1 formalin,

1 silver nitrate, 2 phenol, and 13 fuming nitric acid. One reply stated only that the wounds were washed with aqueous ZEPHIRAN®. The replies for nitric acid also included one hospital which used iodine for facial dog bites and nitric acid for bites elsewhere on the body; one which used either electric cautery or nitric acid; two which listed soap and water cleansing followed by nitric acid, and an additional two which listed both soap and water cleansing and nitric acid except that nitric acid was omitted for dog bite wounds on the face.

The majority of replies stated that their method of treatment coincided with the recommendations of their local public health department; however, five of the hospitals which used soap and water cleansing did so contrary to the recommendation of their local public health department which recommended fuming nitric acid. One hospital in Wisconsin was unique in that it used fuming nitric acid, whereas the local public health department recommended soap and water.

A reply from a Boston hospital stated that they were compelled by state law, and against their own judgment, to cauterize all dog bites with silver nitrate. The reply from another Massachusetts hospital stated there was no such law in their state. One reply from a hospital in New York City stated that there is a New York state law requiring nitric acid cauterization of dog bites, while the replies from four other hospitals in New York stated that there was no such law. Thirty-six replies stated there was no law in their state requiring nitric acid cauterization. Thirteen others did not answer the question or stated that they did not know if there was such a law. It is difficult to believe that there is such a law enforced or in existence in any state. Possibly those who believe there is would find differently on further investigation. Certainly if such a law does exist, the time for its abolishment is long past due.

Included in the replies from the surgical chiefs whose hospitals used nitric acid and who also favored its use personally was one which stated that the writer felt that anyone who did not use nitric acid was leaving himself open to possible medico-legal suit. He further elaborated on the dangers involved in the use of nitric acid, citing a case wherein one patient collected $3000 for an ulcer which developed on a young girl's face following cauterization of a dog bite. It has been stated by a few that before any dog bite on the face is cauterized one should, in the presence of witnesses, explain carefully to the parents or patient, if the latter is of age, the danger of leaving a scar and have them entirely understand that a scar is inevitable, but that with proper care and attention it can be limited to the area of the bite. It has been the experience of these men that by so doing some patients or parents will refuse to have the cauterization done and will sign a release to protect the doctor from legal responsibility regarding further developments and releasing him from the unpleasant necessity of doing the cauterization. It is obvious that both these complicated hazards could be avoided by substituting the more effective soap and water for nitric acid.

It is of further interest to note that among the doctors who use soap and water many of them include the application of antiseptics such as MERTHIOLATE®, zephiran, formalin, iodine, alcohol, ether, zinc oxide, etc., to the wound following the soap and water cleansing. In this way their treatment of dog bites probably varies from that given other soft tissue wounds. Also included in the replies were several statements about dog bite lacerations being left open, packed or loosely sutured, further indicating a failure to classify the rabies virus with other pathogenic aerobic organisms as far as the most effective way to remove them from the wound is concerned.

THERE must be a fairly widespread erroneous opinion that the rabies virus is an anaerobic organism, which it is not, or that dog bites are particularly susceptible to tetanus or other anaerobic infections, which they are not. Of 352 consecutive cases of tetanus previously reported by me,[3] only two gave an antecedent history of an animal bite, which in each instance was of very doubtful etiologic significance. Other reported series show a similar rare etiologic incidence. Similarly, I have never heard of nor seen an anaerobic infection develop from a dog bite wound.

It seems definite that for all practical purposes the possibilities of anaerobic infections from dog bites are minimal or absent. It then follows logically and clearly that there is no possible valid reason for leaving dog bite lacerations unsutured, any more than any other laceration. The existing confusion over this point probably stems from the fact that if these lacerations are

treated with nitric acid, as is mandatory in some places, they are immediately converted into necrotic sloughing wounds which, if sutured, would become secondarily infected.

Several replies stated that nitric acid was used on all dog bite wounds except those on the face. This is, of course, a contradictory practice since it is well established that there is much more danger of rabies associated with a facial dog bite. If the doctor really believes that nitric acid cauterization offers the best protection against rabies, he should feel duty-bound to use it, especially on facial wounds since they, due largely to their shorter incubation period, are more lethal and can receive much less protection from the rabies antisera treatment.

The replies from two large medical center hospitals in Louisville, Kentucky, and Durham, North Carolina, emphasized that their dog bite wounds are treated exactly like any other contaminated soft tissue wound; that is, by soap and water cleansing, debridement, irrigation, and suturing if indicated. It would seem well for all who are concerned with the treatment of dog bites to consider carefully the rationale of such an approach to this treatment problem.

Human bites are different—Because there occasionally develops some confusion between the treatment of dog bites and of human bites, it seems well to add here that human bites constitute a completely different problem of treatment. They are all potentially infected with highly virulent anaerobic organisms with strong invasive and undermining properties and therefore must be treated accordingly.

HISTORY OF CAUTERIZATION

Doctor Samuel Danforth[4] in 1812 is generally regarded as the first to advocate the use of concentrated acid in the treatment of dog bites. In Stockholm, Sweden, in 1824 Ekstrom[5] cauterized, with concentrated hydrochloric acid, the wounds of 106 persons bitten by a known rabid dog. A large percentage of these patients were thereby saved from an otherwise certain death. It was natural then that cauterization was quickly adopted as the treatment of choice throughout most of the world. Gradually nitric acid was substituted for hydrochloric acid as being a more penetrating and effective caustic. In view of the fact that it is now nearly 140 years since this type of treatment was instituted and that since that time our entire present-day knowledge of bacteriology has evolved, together with a completely altered treatment of every other type of soft tissue wound, it would seem well to stop and critically examine the reasons for perpetuating this form of treatment.

In 1899 Cabot[6] showed by experimental work that nitric acid was more effective than silver nitrate and the actual cautery in the prophylaxis of rabies. Poor[7] in 1911 demonstrated experimentally that nitric acid cauterization of wounds provided better prophylaxis against rabies than if no local treatment was given. In 1935 Rosenau[8] demonstrated experimentally the superiority of nitric acid over silver nitrate, phenol, formalin, and the actual cautery. In none of this experimental work was the efficacy of soap and water cleansing compared with nitric acid. However in 1943 Shaughnessey and Zichis,[9] two Ph.D.'s in Chicago, published an article in the *J.A.M.A.* which gives convincing evidence of the superiority of soap and water over nitric acid cauterization in the prevention of experimental rabies. Their work showed that soap and water irrigation, applied thirty minutes after a rabies inoculation, saved 93.8 per cent of experimental animals, as compared to 89.2 per cent of those treated with fuming nitric acid, and 90 per cent of the ones treated with tincture of iodine. Of the animals treated two hours after rabies inoculation, the soap and water saved 85 per cent, the nitric acid 81.3 per cent, and the iodine 60 per cent. In the group treated six hours after inoculation, the soap and water saved 66.6 per cent, while the nitric acid saved 63.3 per cent. No iodine was used on this latter group. The number of untreated controls that survived varied from 36.9 per cent to 27.5 per cent for these three groups.

The description of all the abovementioned experimental work indicates that in each case the concentrated nitric acid was applied deeply, liberally, and without regard for tissue damage. Also, no neutralizing alkaline solution was applied following the nitric acid as is practically universally done in the actual treatment of dog bites. Fortunately, extremely few dog bites on humans today are treated with as thorough an application of the fuming nitric acid as were the wounds of these experimental animals. An experimental survey comparing the efficiency of the degree of nitric acid cauterization usually applied to dog bites and followed immediately by an alkaline neutralizer with the more radical applications applied to these ex-

perimental animals would undoubtedly be very enlightening.

GENERAL DISCUSSION

Many of the doctors who are actually caring for dog bites feel obliged, some perhaps erroneously, to use nitric acid against their own better judgment. They meet the situation by going through the motions of waving a dried-out nitric acid applicator near enough to the wound so that they can legally record it as being cauterized to comply with the letter of existing regulations. Since most of the wounds so treated receive a good soap and water cleansing first, it would seem at first thought to be a harmless though senseless bit of medical ritual; however, as long as nitric acid remains a recognized and, in some places, required form of treatment, there inevitably is going to be a certain percentage of unfortunate individuals who, through the overzealous efforts of a conscientious doctor, or of a nurse treating in the absence of a doctor, or because of an accidental over-application of the acid, will be permanently and needlessly disfigured from this antiquated form of treatment. Most doctors and certainly all plastic surgeons have seen and regret these highly undesirable results. Another definite pitfall is that as long as nitric acid cauterization is used, even in a token manner, there will be a tendency among both nurses and doctors to rely, consciously or not, on the cauterization and thus neglect to do as thorough a soap and water cleansing as might otherwise be done.

It is easy for doctors in public health departments to recommend the cauterization of dog bites. Many of these doctors seldom or never are confronted with an actual dog bite to treat. It is difficult to imagine a responsible doctor caring for a pretty child and feeling complacent about having the frightened child held down while he converts the wounds into acid burns which will leave permanent disfiguring scars. This complacency should be especially lacking if he considers that by so doing he is violating every principle of modern soft tissue surgery, and that in soap and water he has at his disposal a surgically correct, more effective means of treatment.

There is no acceptable evidence that the rabies virus differs in any way from other pathogenic organisms as to the manner in which it is best removed from, or inactivated in, the wound. Since the only way in which a dog bite differs from any other contaminated soft tissue wound is in its potential contamination with the rabies virus, the logical sequence is to treat dog bite wounds like any other soft tissue wound. This conclusion stands solidly on fundamental and undisputably acceptable surgical and bacteriologic principles, and the burden of proof should rightly rest with anyone who disagrees.

It can be said without fear of serious contradiction that not one valid reason has been received for continuing nitric acid cauterization of dog bites. Soap and water cleansing has been proved more efficacious than thorough nitric acid cauterization in experimental animals. It has for several years given satisfactory or superior results in the actual treatment of dog bites in various large medical centers such as University of California, Duke University, University of Michigan, University of Louisville, Cook County Hospital and many others. The inconsistency and deficiency of using nitric acid or other caustics either routinely or for especially deep, suspicious, old or non-facial bites thus becomes quickly apparent. The only way in which nitric acid acts against the rabies virus is by complete destruction of all living tissue with which it comes in contact. It is readily admitted and well proved that nitric acid applied thoroughly will effectively destroy the rabies virus along with all other living tissue with which it comes in contact. This destruction of all virus can take place only if an amount of acid sufficient to cauterize thoroughly all parts of the wound is used. This cannot be reliably accomplished by a scanty amount of nitric acid on small applicators or on applicator sticks, followed by immediate neutralization. It is apparent that if all adjacent living tissue is not destroyed it must be assumed that neither is all the virus destroyed. Furthermore the living virus that may be left is thus provided with an ideal culture media of necrotic tissue in which to grow and multiply. It seems clear then that doctors who use nitric acid on dog bites must fit into one of two categories. Either they do not cauterize adequately to insure destruction of all virus or they apply sufficient acid to insure deep and permanent scars. I strongly doubt that a safe compromise between these two end results is or can be consistently followed.

Those who believe that nitric acid will penetrate the entire depth of the wound better than soap and water are disagreeing with the funda-

mental accepted principles of all other types of traumatic surgery. If a puncture or otherwise inaccessible wound exists, it can be enlarged, cleaned to its depths, debrided and sutured. If the wound is old or strongly suspicious of rabies it is a far more logical surgical procedure to excise the entire area and leave a clean surgical wound, sutured if possible, than to convert the entire surrounding area, by means of fuming nitric acid, into a sloughing mass of necrotic tissue.

This is not by any means a new presentation of this problem. Several articles[10-12] in recent years have been published convincingly condemning the use of caustics. There is no doubt but that the use of caustics on dog bites is steadily and surely declining. It is a matter of regret that in the presence of such overwhelming evidence the decline is so slow and is contested so stubbornly in certain quarters, particularly by personnel of various public health agencies.

REFERENCES

1. Virus Diseases of Man. 1940, Oxford University Press, p. 669.
2. Control of rabies in Istanbul. J.A.M.A. 142:437 (February 11) 1950.
3. Vinnard, R. T.: 352 cases of tetanus. Surgery 18:482 (October) 1945.
4. Thatcher, James: Observations in Hydrophobia. 1812, Joseph Avery Co., p. 239.
5. Ekstrom, F. A.: 1830 rabies epidemic at Stockholm in 1824. London M. Gaz. 6:689.
6. Cabot, F.: The cauterization of wounds infected with the rabies virus after an interval of 24 hours. M. News 74:329-331, 1899.
7. Poor, I. W.: The late cauterization by means of nitric acid of wounds infected with rabies virus. 1911, Collected Studies from the Research Laboratories, Dept. of Health, City of New York, p. 625.
8. Rosenau, M.: Preventive Medicine and Hygiene. Ed. 6. New York, Appleton Century Co., 1935, p. 353.
9. Shaughnessey, H. J. and Zichis, J.: Prevention of experimental rabies. J.A.M.A. 123:528, 1943.
10. Sellers, T. F.: Personal communication to the surgeon general, U. S. Navy, January 21, 1947.
11. Chieffelle, T. L.: J. Tennessee M. A. 39:14 (January) 1946.
12. Johnson, H. N.: Presented at conference on "The Relation of Diseases in the Lower Animals to Human Welfare," New York Academy of Science, March 1946.

COMING POSTGRADUATE COURSES

University of Minnesota Medical School, Minneapolis

Continuation course in child psychiatry for general physicians and pediatricians, November 26-December 1. Visiting faculty members will be Dr. Reginald S. Lourie, Washington, D. C., and Dr. J. Franklin Robinson, Wilkes-Barre, Pennsylvania. Dr. Reynold A. Jensen, Departments of Psychiatry and Pediatrics, is chairman for the course.

Continuation course in fractures and traumatic surgery for general physicians and surgeons, November 8-10, at the Center for Continuation Study.

University of Colorado School of Medicine, Denver

Postgraduate course in heart disease, November 15-17, sponsored by the Colorado Heart Association and the State Department of Health. Visiting faculty members for the course will be Dr. Paul D. White, Boston, Dr. Gordon B. Myers, Detroit, and Dr. John P. Hubbard, Philadelphia. A 3 day course in clinical electrocardiography at the Fitzsimons Army Hospital on November 12-14 will be open without cost to any physician attending this symposium.

Diagnosis and management of patients with poliomyelitis, December 13-15.

Tufts College Medical School, Postgraduate Division, Boston, Massachusetts

Courses for the General Practitioner

Ophthalmology, 4 weeks, mornings, Mon., Wed., Fri., January 7-February 1
Electrocardiography II, full time, 3 days, January 14-16
Rheumatic Diseases, full time, 3 days, February 4-6
Neuro-ophthalmology, full time, 5 days, March 3-7
Diabetes, full time, 3 days, March 10-12
Cardiology, full time, 5 days, March 17-21
Dermatology II, full time, 5 days, April 7-11
Proctology I, full time, 5 days, April 21-25
Traumatic Surgery, full time, 2½ days, April 24-26
Proctology II, full time, 4 weeks, April 28-May 24

American College of Chest Physicians

Interim session, December 2 and 3, at the Ambassador Hotel, Los Angeles, California. Dr. Edward W. Hayes, Monrovia, California, is chairman of the general arrangements committee, and Dr. Alfred Goldman, Beverly Hills, is chairman of the scientific program committee.

Pediatrics

IN GENERAL PRACTICE

For general practitioners, in whose practice is included a major proportion of the medical management of infants and children, and for the specializing pediatrician as well, POSTGRADUATE MEDICINE *presents this special regular department devoted to brief discussions by recognized authorities on their preferred methods of the treatment and management of diseases and problems of infancy and childhood.*

Congenital Hernias in Infancy and Childhood

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CAULFIELD

THE most common types of hernias found in children are of the congenital variety, and of these the inguinal and umbilical far outnumber those of any other region such as the diaphragmatic, intraperitoneal, obturator or femoral. The former two are those most frequently operated on by the occasional operator; the latter are usually taken care of by specialists.

Inguinal hernias—Inguinal hernias in children are of the indirect variety and, therefore, possess a distinct sac associated with the cord and protrude through the internal inguinal ring. The sac may be retained within the inguinal canal or it may be continuous with the tunica vaginalis of the testicle, because of failure of closure of the processus vaginalis. Frequently the hernia may be associated with a hydrocele, and for this reason it is well never to operate on a hydrocele in a child without investigating the inguinal canal. Most hernias in children will reduce themselves when the child reclines, but hydroceles never do except on rare occasions, where a pinpoint opening exists between the hydrocele and the accompanying hernial sac. This allows the fluid to empty slowly into the abdominal cavity.

The diagnosis of hernia in small children is usually made by inspection because the examining finger cannot be inserted into the inguinal canal. It is well for the surgeon not to rely upon the word of the parents alone that the child has a "bulge" in the groin. He should make every effort to determine the presence of the hernia, and sometimes this may take two or three visits to his office. When a hernia is complete or incarcerated, it is then self-evident.

TREATMENT

When the diagnosis of hernia has been made, the treatment will be a choice between the wearing of a truss or operation. In our experience the wearing of a truss by an infant or child is a

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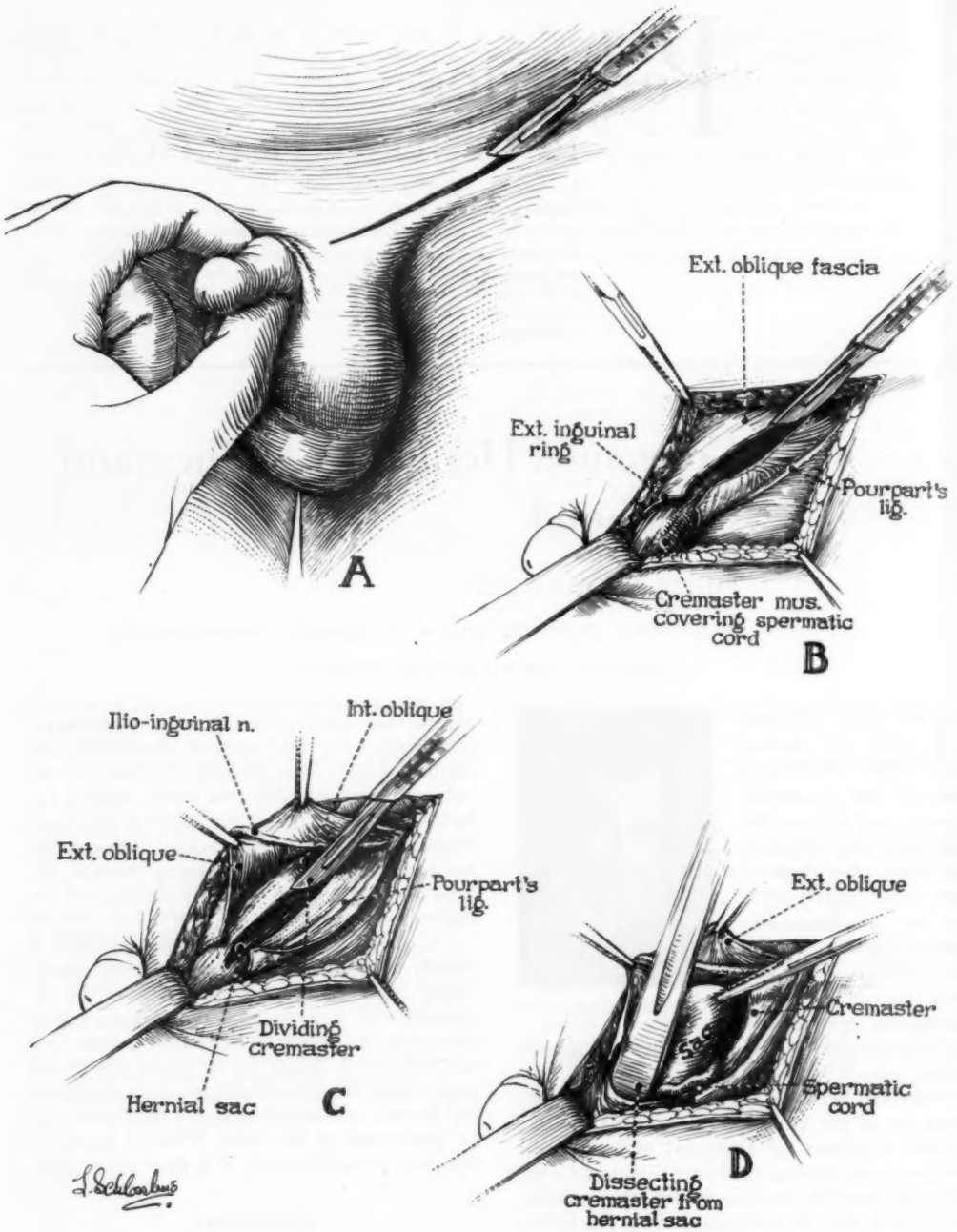

FIGURE 1. (a) Skin incision made from base of penis oblique outward. (b) Splitting of fascia of external oblique from apex of external ring exposing cremaster muscle lying over cord. (c) Splitting of cremaster by sharp dissection and exposing the cord with sac attached. (d) Freeing of hernial sac without displacement of cord from inguinal canal.

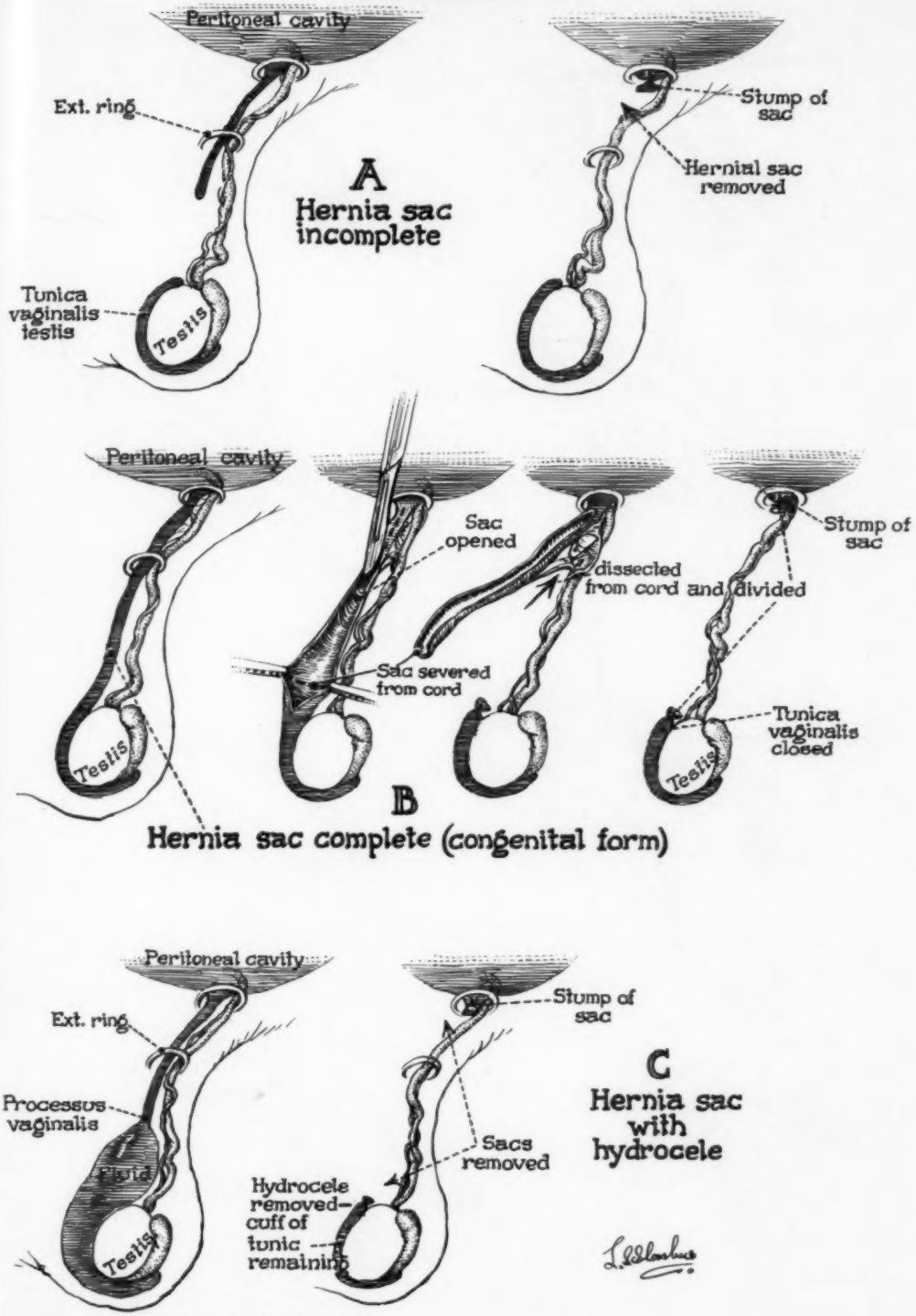

FIGURE 2. Hernial sacs and technic of removal.

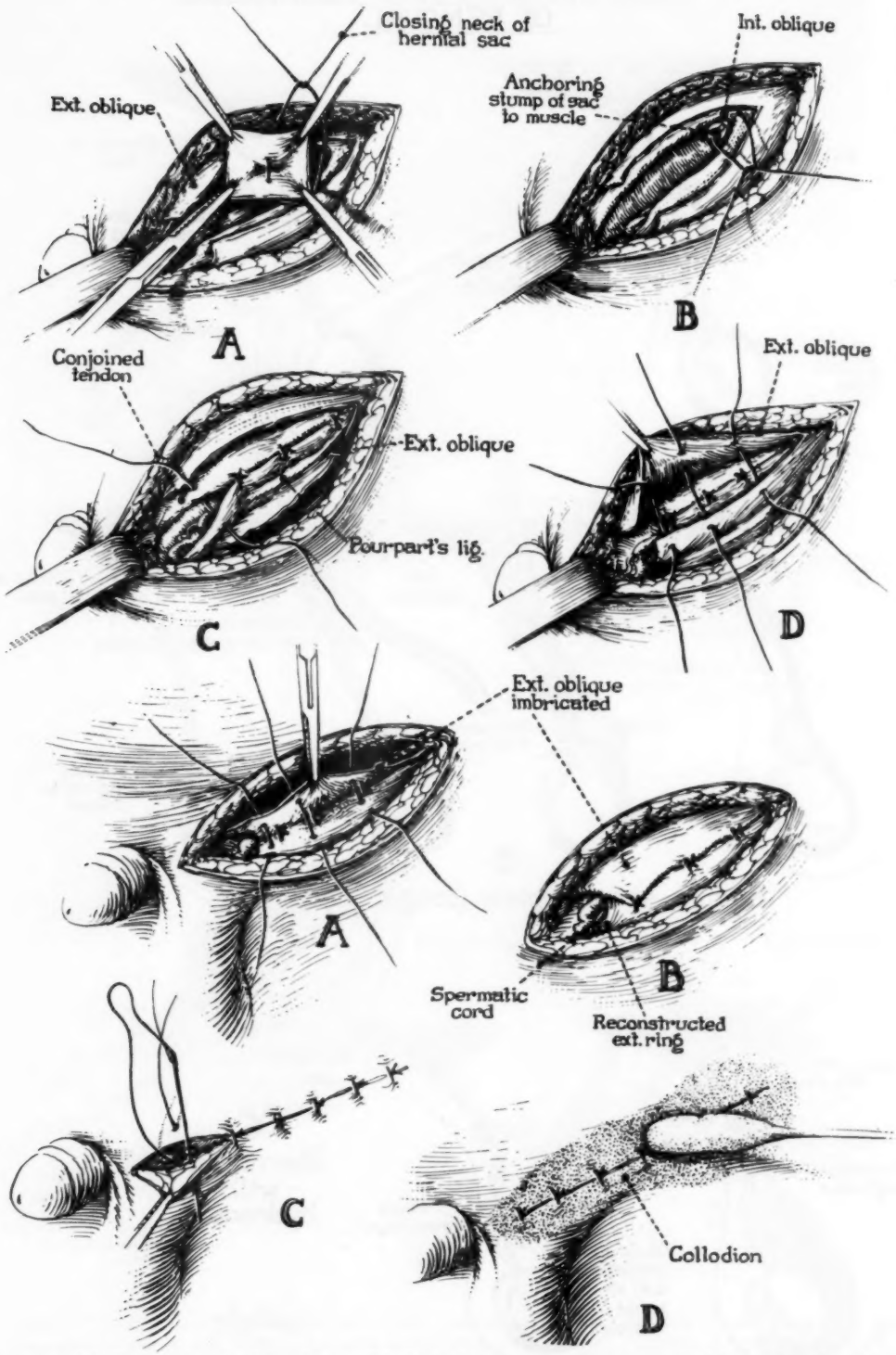

FIGURE 3. (a) Closing of neck of hernial sac. (b) Anchoring of stump of sac to muscle. (c) Suturing of conjoined tendon to Poupart's ligament directly over cord. (d) Beginning of imbrication of fascia of external oblique.

FIGURE 4. (a and b) Completion of imbrication of fascia of external oblique over cord. (c and d) Suturing of skin and application of collodion dressing.

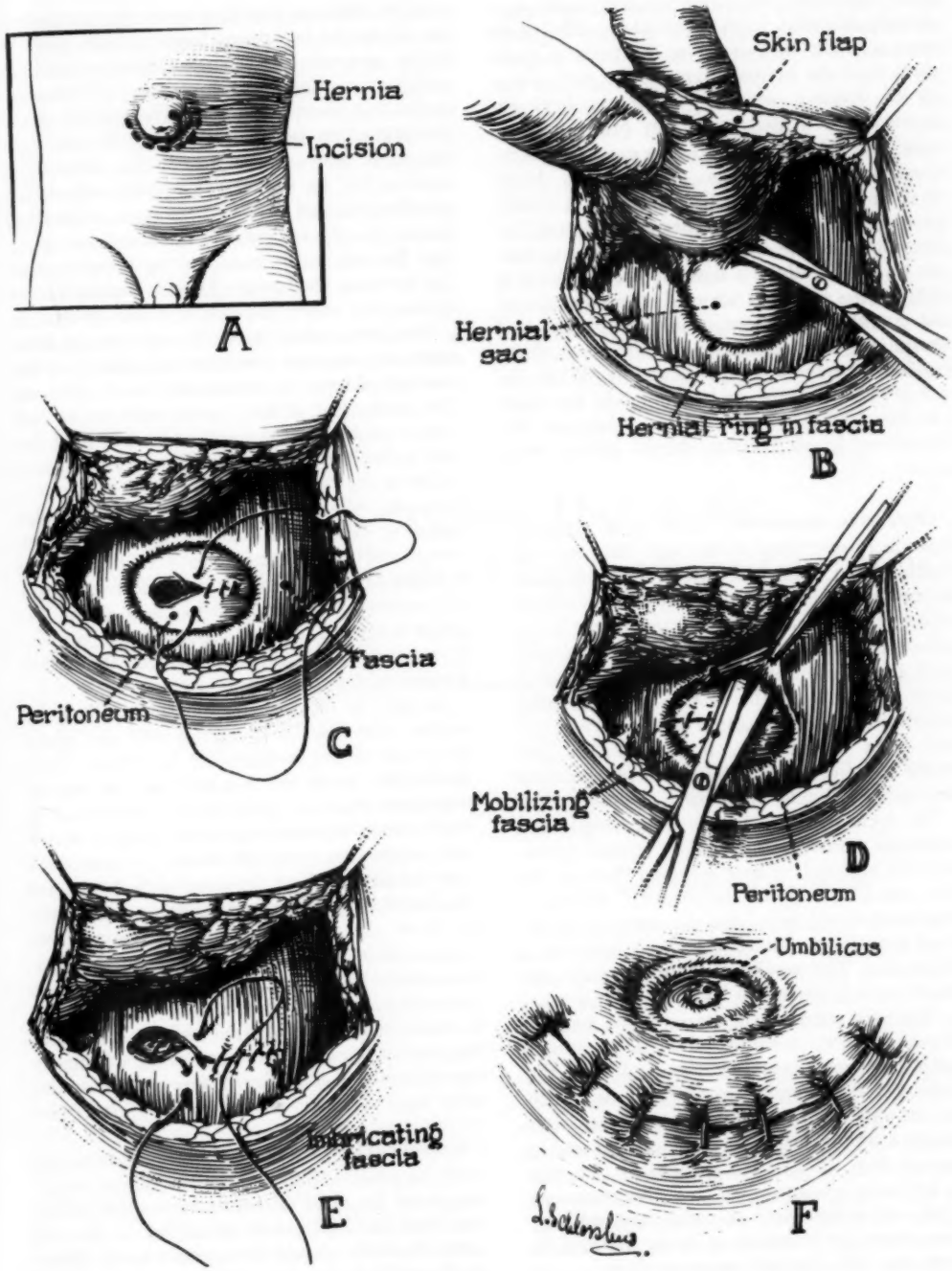

FIGURE 5. Technic of umbilical herniorrhaphy.

most uncomfortable, unsatisfactory and occasionally harmful form of therapy. All trusses need constant adjustment to the body to make them hold the hernial mass. In the vast majority of children wearing trusses we have examined, the hernial mass was protruding beneath it, and we have also seen cases where the truss caused incarceration of the hernia. Many of these children were the offspring of intelligent and careful parents. Because of these factors and since the operative treatment is so safe, we no longer advise a truss. If the operation is delayed the hernia is allowed to protrude, and the parents are instructed about the signs and symptoms of incarceration. We have had no trouble by following this procedure. With the aid of the telephone and automobile the child can be quickly transported to a hospital for immediate herniorrhaphy, should incarceration occur.

Operative treatment—There is no contraindication to operating at any age. However, the cord and the canal of Nuck are very small in infants and children, and injury to the vas deferens or to the fallopian tube and ovary occurs more frequently. It is, therefore, better to wait until the period of infancy is over—that is, about 12 to 18 months. If the hernia becomes incarcerated or strangulated it should be operated upon immediately. If it constantly protrudes and the parents become very apprehensive, surgery should be advised.

The operative procedure is quite simple and consists of a modification of the Ferguson operation. An inguinal incision is made through the skin, and the fascia of the external oblique is then cleaned and split from the apex of the external ring for a distance of about one and a half inches. The small ilio-inguinal nerve can then be seen lying on the internal oblique muscle. The split edges of the fascia of the external oblique are then retracted and the cremaster muscle is opened revealing the cord with the hernial sac. No attempt should be made to displace it and the sac should be grasped, after opening it and reducing its contents, and gently dissected free. If it is an incomplete sac this can be easily accomplished and the neck can be tied and severed and no effort at transfixing of the stump is necessary, it being allowed to retract into the internal inguinal ring.

If the sac is complete, it will be continuous with the tunic of the testicle. This will require a little different handling than the incomplete sac. It should be opened longitudinally and the edges grasped with clamps, tightly stretching it. Using a sharp scalpel, the sac is then transected just above the testicle. The portion of the sac remaining below will be continuous with the tunic and can be closed, thus forming a new sac for the testicle. The portion above can then be dissected free from the cord as described before. Great care must be exercised not to injure the vas in the male, or the fallopian tube and ovary in the female. The ilio-inguinal nerve is also very small and can be easily injured.

After removal of the sac no attempt should be made to close the cremaster; the fascia of the external oblique is imbricated above the cord. The under leaf of fascia is sutured to the conjoined tendon and the outer leaf laid over this and sutured to it. Just enough space is allowed below at the pubic tubercle to allow the cord to protrude without strangulation. A #00 Dulox suture is ideal for this closure. The skin is then closed with a fine #36 wire suture or cotton. Silk has a tendency to become infected because of contamination from urine and feces. No gauze is applied to the wound; the area is merely painted with collodion which allows the wound to be kept dry and clean.

As soon as the child is able, he is allowed a regular diet and to be out of bed and about his room. If his temperature is normal he is discharged from the hospital on the second postoperative day and the parents instructed to restrict him only from violent or excessive activities. Sutures are removed in five to seven days.

In the female child, the canal of Nuck is very small and it is almost impossible to remove the sac from the underlying round ligament. No harm is done in ligating and severing this ligament with the sac. Here, instead of allowing the sac to retract through the internal ring, it should be transfixed to the internal oblique muscle at the edge of the ring, thus supporting the uterus on the involved side. The repair is otherwise the same as in the male.

Umbilical hernias should be treated conservatively by pressure over the protrusion and strapping until the child is about one year old. If at this time no appreciable reduction in size is noted, the child should be operated upon. Most small umbilical hernias will close as the child grows older, but large hernias seldom close even when strapped. The strapping must be of

adhesive tape, for a tight binder will not hold. A coin or some small object can be placed in the deficiency and the tape applied over it and allowed to remain in place until it becomes loose. Frequent changing of the tape irritates the skin. Painting the skin with tincture of benzoin or collodion before the tape is applied will lessen this irritation.

Umbilical hernias in males should not be repaired except where they are very large and cause symptoms. In females, however, all umbilical hernias existing after one year of age should be repaired because future pregnancies may aggravate it. The surgical procedure consists of making an elliptical incision of the skin on one side of the navel and elevating it from the surrounding fascia. As it is elevated, the sac of peritoneum attached to it will also be brought out and the edges of the fascial deficiency can be easily identified. The peritoneal sac can then be cut free from the umbilicus, the contents reduced, the neck ligated and the sac removed. The fascial edges of the linea alba are then sutured transversely without separating them or trying to overlap them. Only in rare instances when the opening is very large is imbrication necessary. Two or three #8 cotton sutures placed through all layers of fascia will close the deficiency. The skin with the umbilicus is then sutured over this area and an adhesive dressing is applied to the wound. The child can be discharged from the hospital on the second postoperative day, and the sutures are removed on the fifth or sixth day.

The Ketogenic Diet in the Treatment of Epilepsy in Children

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Fasting has been a common method of treatment of epilepsy through the ages. It is suggested as a treatment in the New Testament, as shown by the following quotation which referred to an epileptic child, "This kind goeth not out but by prayer and fasting." (Mark 9:24.)

The good results of fasting led Wilder to attempt to reproduce the ketosis and acidosis of starvation by means of a constant high fat diet, and in 1924 he introduced the ketogenic diet as a treatment for epilepsy. Many observations since that time have established its usefulness in certain forms of epilepsy.

MECHANISM OF ACTION

The exact mechanism of action of the ketogenic diet is still unsettled. It is thought, however, to be due to a combination of the following physiologic effects: (1) a mild degree of acidosis; (2) the sedative action of the ketone bodies, and (3) dehydration and the loss of fixed base.

SELECTION OF PATIENTS

Although there is some diversity of opinion as to the type of epilepsy that is most likely to respond to the ketogenic regimen, many pediatricians consider the ketogenic diet the treatment of choice for children with epilepsy of any type.

It has been our experience that the ketogenic diet gives the best results with children between the ages of 3 to 5 years who have grand mal seizures and/or petit mal spells of the akinetic variety and who present electrocardiographic abnormalities consisting of slow spike and wave forms. Favorable results are occasionally obtained with patients up to 8 years of age, but beyond this age it is rarely successful since it is difficult to maintain an adequate state of acidosis and ketosis in the older children.

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It should be remembered that even though the patient's condition is one which ideally may be treated by the ketogenic diet, this treatment may not be ideal for the particular case. One must be dealing with cooperative, moderately intelligent parents who will consider maintenance of the diet seriously and adhere to it religiously.

Once started, the diet must be followed closely or its entire beneficial effect is lost. Therefore, one wastes time attempting such a regimen with a completely undisciplined child who controls the elders in his family or with a child for whom adequate supervision cannot be maintained. Similarly, it is of little use to begin a ketogenic diet if the parents are not sufficiently intelligent to understand the relatively simple method of weighing the dietary components and varying the diet. The parents also should understand that the high fat content of the diet makes it cost about twice as much as an average normal diet.

On the other hand, the advantages of the ketogenic diet regimen are, first, that it is most often successful in controlling seizures in properly selected cases. Second, it is the only anticonvulsive therapy in which any significant number of patients shows a reversion of the electroencephalogram to normal; finally, a higher percentage of patients remains free of convulsions following discontinuance of the diet than do those on other forms of therapy.

PRELIMINARY FASTING PERIOD

Prior to starting the ketogenic diet, four or five days of starvation are necessary. For this reason the patients must be under close observation; hospitalization is usually necessary.

The patient receives nothing by mouth except 800 to 1000 cc. of water daily. Since dehydration plays a therapeutic role, the fluid intake should not exceed this amount. On the other hand, less than this amount will cause the patient to become excessively dehydrated.

If the patient has been receiving anticonvulsive medication, this should not be terminated abruptly. If phenobarbital forms part of the therapeutic regimen, it is usual to discontinue all other drugs at the beginning of the starvation period but to maintain the phenobarbital dosage until the day of the first ketogenic diet meal and thereafter to eliminate it gradually over the next two weeks. If the patient is being treated without phenobarbital but with other drugs, these are reduced in amount daily, beginning with the first starvation day and are eliminated at the end of the preliminary starvation period.

During the period of starvation, the child may be up and around and should be encouraged to participate in ward play activities. For obvious reasons he should not be present when meals are served to other children. He must be observed closely for untoward signs of acidosis or dehydration. The pulse rate should be counted every four hours after a short period of rest in a recumbent position. If the pulse rate exceeds 120 per minute at rest, the patient should receive an intravenous injection of 200 cc. of 5 per cent dextrose solution.

Patients frequently complain of nausea, usually during the second or third day of starvation at which time the acidosis and ketosis have usually reached their peak. When this occurs, the patient is put to rest and encouraged to take cracked ice by mouth. If the nausea persists, he may be given 60 cc. of orange juice. This amount will usually relieve the nausea and, although it diminishes the degree of ketosis, it does not materially affect the desired results of starvation.

The urine is examined for acetone and diacetic acid twice daily. Blood sugar levels are determined daily. Should the level fall below 50 mg. per 100 cc., the patient should receive 200 cc. of 5 per cent dextrose solution intravenously or 60 cc. of orange juice by mouth.

The child is weighed at about the same time each day. To minimize fluctuations in weight, water is withheld for the preceding two hours and the child is asked to void just before being weighed. During the first few days of starvation, the daily weight loss is usually great and irregular, but it becomes more or less constant by the fourth or fifth day. When, after the third day of starvation, the weight loss on two consecutive days has been essentially the same and the tests for acetone and diacetic acid in the urine are strongly positive, the ketogenic diet may be started.

CALCULATION OF DIET

A simplified method of calculating the ketogenic diet is used. The child must (1) receive the number of calories per day required to maintain growth and (2) receive these calories

in the proposed ketogenic-antiketogenic ratio.

1. The number of calories required per day is calculated by multiplying the child's weight (in kilograms) by the average number of calories per kilogram required daily. For the age group treated by ketogenic diet, this is 70 calories per kilogram per day. Undernourished children and those with poor appetites are started on less.

2. Although not strictly true, it is quite feasible from the practical standpoint to consider all of the fat in the diet as ketogenic and all of the protein and carbohydrate as antiketogenic. For convenience, calculation of the diet is made using what we term the *dietary unit*. A unit represents the relative quantities of the ketogenic to antiketogenic ingredients of the diet. Thus a unit of the usually employed 4:1 diet contains 4 gm. of fat and 1 gm. of carbohydrate plus protein. Since each gram of fat yields 9 calories and each gram of protein or carbohydrate 4 calories, this unit will yield a total of 40 calories.

The number of calories the child requires per day (as calculated in [1]) is divided by 40 (the number of calories per unit as calculated in [2]). This gives the number of dietary units required daily.

Example—A five year old child weighing 18 kilograms is to be put on a diet of the 4:1 unit type.

18 kilograms x 70 calories per kilogram = 1,260 calories per day.

1,260 calories per day ÷ by 40 calories per unit = 31.5 units.

In a 4:1 diet, each of these units contains 4 gm. of fat. Therefore, the number of grams of fat can be calculated by multiplying the number of units (31.5) x 4 = *126.0 gm. of fat required for the daily diet.*

EACH dietary unit contains 1 gm. of protein plus carbohydrate. It is important, however, that these children receive enough protein to maintain proper growth. This requirement is approximately 1 gm. of protein per kilogram of body weight. Therefore, the body weight in kilograms is multiplied by 1 gm. per kilogram to obtain the required number of grams of protein; that is, 18 kg. x 1 gm. per kilogram = *18 gm. of protein required for the daily diet.* The remainder of the diet is then made up of carbohydrate. This is calculated by subtracting the computed number of grams of protein from the number of dietary units; that is, 31.5 units – 18 gm. protein = *13.5 gm. of carbohydrate required for the daily diet.*

This 4:1 diet calculated in the example would then be:

Fat	126 gm.
Protein	18 gm.
Carbohydrate	13.5 gm.

An alternative method may also be used for rapid calculation of a 4:1 ketogenic diet. It happens that the number of *grams* of fat required is one-tenth the number of calories needed per day. In the example used, 1,260 calories per day require one-tenth of 1,260 or *126 gm. of fat.* Each gram of fat yields 9 calories; 126 gm. x 9 calories per gram = 1,134 calories in the form of fat. Subtract this from the total number of calories—1,260 – 1,134 = 126 calories to be supplied in the form of protein plus carbohydrate. Since both protein and carbohydrate yield 4 calories per gram, the number of grams of these two combined is calculated by dividing the number of calories by four: 126 ÷ 4 = 31.5. But, as already described, a child needs 1 gm. of protein per day for each kilogram of body weight. Thus the child weighing 18 kg. needs *18 gm. of protein per day.* Subtract this figure from the total grams of protein plus carbohydrate to determine the number of grams of carbohydrate—31.5 – 18 = *13.5 gm. of carbohydrate.*

Calculated diet:

Fat	126 gm.
Protein	18 gm.
Carbohydrate	13.5 gm.

The total daily caloric requirement is usually given in three equal meals at usual mealtimes. The distribution of calories in the three meals may, however, be varied to suit individual cases as long as the total number of calories per day remains the same. For the first meal given on the ketogenic regimen, it is advisable to offer only half the calculated number of calories to avoid upsetting the previously fasting gastrointestinal tract.

The ketogenic diet is rich in the fat-soluble vitamins A and D but is deficient in the water-soluble B and C complexes and in calcium. Therefore, it is advisable to supplement the diet with the daily administration of 50 mg. of ascorbic acid, 1 gm. of brewer's yeast and 2 gm. of calcium gluconate daily.

Patients begun on ketogenic diets almost al-

ways complain of hunger between meals for the first several weeks, even though the caloric intake is adequate. This is largely due to the fact that, because of the high fat content, the bulk of a ketogenic diet is considerably less than that of a normal diet of the same number of calories. The temptation to increase the diet should be resisted because the stomach will adjust to the lesser bulk in about two weeks and because patients will often refuse to eat all of such a high fat diet unless kept hungry until they have become accustomed to it. It is obvious that the diet will be successful in maintaining ketosis only if all of it is eaten.

Problems of hunger, rewards, etc. can usually be solved by permitting the child to partake of the non-nutritious gum drops and other products sold for diabetic persons, such as Cellucandies.

Since the entire efficacy of the ketogenic regimen rests on maintenance of ketosis, the urine should be tested for the presence of acetone and diacetic acid daily. Parents can be supplied with materials and instructions to perform these tests at home. Although the amounts of acetone and diacetic acid in the urine may fluctuate slightly, any consistent diminution requires investigation. The usual cause is consumption of stolen sweets or other foods and indicates the need for increased vigilance. Occasionally, excessive use of even noncarbohydrate candies seems to blame. It must constantly be borne in mind and the fact impressed on the parents that ketosis must be maintained in order to be effective and that once lost it is difficult to regain.

If the ketogenic diet proves to be a satisfactory therapeutic regimen, it should be maintained at 4:1 ratio for two years. The indications to abandon the regimen are: (1) failure to maintain ketosis, either for lack of cooperation or other reasons; (2) failure to affect favorably the frequency or severity of the seizures and (3) insurmountable psychologic obstacles in the form of behavior problems.

After two years on the 4:1 diet, it may be reduced to a 3:1 ketogenic-antiketogenic ratio. The method of calculation is similar to that described for the 4:1 diet except that each dietary unit contains 31 calories instead of 40 (3 gm. fat x 9 = 27 + 1 gm. of protein-carbohydrate x 4 = 31). Therefore, the number of grams of fat required must be the number of dietary units multiplied by 3. The number of grams of protein is calculated as for the 4:1 diet, that is 1 gm. of protein per kilogram of body weight. The number of grams of carbohydrate is computed by subtracting the grams of protein from the number of diet units.

The patient is continued on the 3:1 diet for three months after which a 2:1 ratio is substituted. The calculation is as follows: The dietary unit now contains 22 calories (2 gm. fat x 9 calories = 18 + 1 gm. carbohydrate-protein x 4 = 22 calories). The number of dietary units is multiplied by 2 to give the number of grams of fat required. On a 2:1 diet it is feasible to give 1½ gm. of protein per kilogram of body weight. This calculated number of grams of protein subtracted from the number of dietary units gives the grams of carbohydrate.

After three months on a 2:1 diet, the patient may be given a normal diet as desired. During the period of reduction of the ketogenic-antiketogenic ratio, there will be a progressive diminution in the degree of acetonuria. This may be disregarded and testing of the urine may be discontinued after acetone is no longer present. The main object of the gradual reduction in the ketogenic-antiketogenic ratio is to lessen the likelihood of inducing status epilepticus.

During the period the child is on a ketogenic diet, the parents should be warned and the physician should remember that *no carbohydrate-containing medications, such as elixirs or syrups, should be given.*

If during an illness the patient refuses or should not take solid foods, the diet is temporarily discontinued and the child given liquid nourishment in the form of special eggnog. For the 4:1 diet, this is made as follows:

Dissolve ¼ gr. of saccharine in a teaspoon or two of water and add to 60 gm. of 36 per cent cream. To this mixture add 20 gm. of lightly beaten raw egg and 10 drops of vanilla. A little nutmeg may be sprinkled on top if desired.

Case Report

Clinical Management of a Male Pseudohermaphrodite

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The authors describe a male pseudohermaphrodite who wanted to be more feminine in appearance and who was treated accordingly, both endocrinologically and surgically. The ramifications of such a regimen are discussed.

Minor abnormalities of male genital development are not uncommon in clinical practice. Hypospadias, even when marked, may be consistent with satisfactory sexual activity. Occasionally however the hypospadias may be of such magnitude that the external urethral orifice opens just anterior to the anus. Under such circumstances, the scrotum is usually bifid, the testicles abdominal, and pink, moist, mucosal folds, resembling the labia minora, are present on each side of the urethra. The penis is small and concealed between the halves of the bifid scrotum.

It is not unusual for such patients to be mistaken for females at birth, and many of them are, in fact, reared as girls. With the advent of puberty, however, the genetic sex of the individual becomes manifest and it is at this time that problems of management arise.

Confronted with data which conclusively establish their genetic masculinity, most such patients choose to be identified as males, and request necessary treatment, both medical and surgical, to accomplish this end. The role of the physician in this situation is clearly to help his patient approach somatic normality as closely as possible. The problem raised by the male pseudohermaphrodite who prefers to live as a woman is much more perplexing from both the psychologic and the physical points of view. The purpose of this presentation is to describe just such a dilemma, to explain how it was handled, and the reasons for following this type of management.

K. R., a 15 year old white girl, was referred to one of us by Miss Doreen Moore of the Family Society because of the recent development of certain masculine traits, including change of voice and facial hair growth. The lack of breast enlargement and absence of menstruation at this age, in addition to the general suspicion that something was wrong with her behavior, gave rise to considerable concern among her teachers and fellow students. Working papers were to be issued to her, and the authorities were sufficiently in doubt about her true sex as to request further medical investigation. The patient was completely convinced of her own femaleness and dressed and acted accordingly. She spoke in a soft, well modulated voice, wore her hair long, used rouge and lipstick, and appeared to be overly graceful in her movements and gestures.

During the interviews, in which K. was relatively inarticulate, the psychiatrist was impress-

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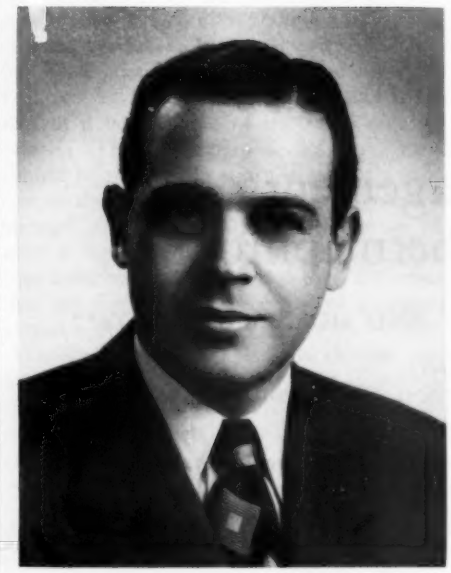

WILLIAM H. PERLOFF

ed by the emphasis on feminine interests such as dolls, sewing, cooking and keeping house, and the exaggeration of feminine mannerisms. K. was extremely disturbed when her voice would break in typical masculine pubertal manner, was aware of a "piece of skin" which she guessed was her "male part," but claimed she "didn't like to think about it." Her effort to impress everyone with her femininity characterized her behavior. She spoke of strong sexual feelings and an urge to be penetrated. She repeatedly expressed the wish to be married and to have children. There were recurring dreams of marriage and childbirth. Frequently the dreams involved giving birth to twins.

In 1947 the patient had been subjected to laparotomy at another hospital where absence of the appendix, uterus and ovaries was reported. Small, atrophic, abdominal testicles were found, and the true nature of K.'s sex was explained to her. Despite this incontrovertible evidence, K. refused to entertain the notion that she might be masculine, and the psychiatrist finally concluded that better insight was unobtainable and agreed that the patient should be treated as a female.

K. had been raised by relatives since neither parent would accept the responsibility of her care. She has two brothers, one of whom is a delinquent; the other is in reform school. The Wechsler-Bellevue test showed dull normal intelligence with an I.Q. of 80. A Rorschach test was unrevealing because the patient was uncommunicative.

She was admitted to the surgical services of Drs. William Erb and L. K. Ferguson, of the Philadelphia General Hospital, for further study and treatment. At this time she gave the impression of being a masculine-appearing young woman with thick axillary and pubic hair. The genital organ was 1 inch in length and resembled an enlarged clitoris. The scrotum was bifid and looked like female labia, and in each side a small pea-sized nodule could be felt, which was interpreted as being an atrophic testicle. No breast tissue was palpable and there was a slight growth of facial hair, particularly on the upper lip and chin. The verumontanum and prostatic lobes could not be located. The bladder was normal, but a blind diverticulum was found leading from the posterior urethra, which opened in the perineum just anterior to the anal orifice. An intravenous urogram showed normally functioning kidneys. The pelvis was reported as "gynecoid" by x-rays; the bones of the skull and sella turcica were described as normal. Physical examination was otherwise irrelevant.

A 24 hour urinary bioassay revealed estrogens of 13 mouse units, gonadotropins of over 125 mouse units, and 17-ketosteroids of 4.8 mg. This is a typical castrate-type hormonal excretion, so that the patient appeared to be genetically male, hormonally castrate, but psychologically female. Routine laboratory studies were normal.

After repeated consultation among the psychiatrist, endocrinologist and surgeon, it was decided to accede to the patient's request to remain a female, and accordingly on December 8, 1948 the atrophic testicles were removed and a 25 mg. pellet of compressed estradiol implanted into each labium. An exterior vaginal tract was created employing the loose scrotal folds. Dr. William E. Erich, pathologist, reported the testicles as showing complete underdevelopment of the seminiferous tubules which were separated by masses of degenerated interstitial cells. No spermatogenic elements were observed. Assay for hyaluronidase revealed none of this material in the testicles.

By December 17, 1948 the breasts and areolae

were showing signs of growth and development. The genital organ was smaller and there had been some loss of facial hair. A bioassay revealed 54 mouse units of estrogen, no gonadotropins, and 5.4 mg. of 17-ketosteroids. These changes were progressive so that by March 18, 1949 the breasts appeared to be normal, well developed, postpubertal female breasts. The urinary bioassay on September 7, 1949, nine months after pellet implantation, showed 44 mouse units of estrogen, no gonadotropins, and 5.7 mg. of 17-ketosteroids—demonstrating that the estrogen pellets were still hormonally active. The breasts and genital organ had not changed since the examination in March and therefore maximum effect was inferred to have occurred.

At this time the patient was re-evaluated by the psychiatrist and social worker. K. was extremely grateful for the help she had received and, for the first time, appeared quite friendly. She had become engaged to be married and was having heterosexual intercourse. She wanted to know if she could become pregnant, despite repeated previous explanations to the contrary. She claimed that sexual desire had increased since the operation, but that the "male part" became hard and interfered with the sex act. Because of this, she requested that it be removed. So far as could be determined, the center of sexual tension was in the "clitoris" and not in the surgically created vagina. This appeared to be confirmed by the increasing erection and masturbation of this organ postoperatively.

The Rorschach studies were repeated by an examiner who was unacquainted with the patient or her problem. He reported: "There is a tendency towards evasion and an excessive preoccupation with material and animal phenomena. Limited variation in ideas and a high proportion of time and effort expended in childlike fantasy, without the real animation necessary for executing these ideas, give the impression of dullness in intellectual functioning which may be mistaken for primary intellectual insufficiency . . . Perhaps the most severe basis for conflict, a condition which may be close to consciousness because of rather naive symbolism, is her very apparent trauma concerning appendages or phallic-like structures . . . Identification is with the female and includes characteristic flexor-submissive attitudes. However, there is marked disturbance when she is required to reflect on somatic structurization as in the 'Draw-A-Person' test. Here she has considerable difficulty, probably because she cannot reflect upon her own sexuality and because both male and female associations are disturbing."

MORRIS W. BRODY

DISCUSSION

The problems raised in the management of this individual are interesting and perplexing at the same time. Shall one follow the wishes of the patient himself, or shall nature's ineffective intent be the motivating influence? Obviously, the final decision cannot be up to the patient. In effect, K. R. was a homosexual male who desired to be a female. With the medical tools presently available, we were able to fulfill this wish in modified fashion. If this procedure were carried out ad absurdum, genetic males, normal physically, who were homosexual, might present themselves for such treatment. Manifestly, no reputable physician would be a party to such manipulation, and yet, in effect, the present authors were guilty of just such behavior. It is true that in this instance physical abnormalities may have provided extenuating circumstances, since there had been some doubt about this patient's true physical sex since birth. The prime error was made when the child was first examined as an infant. The correct diag-

nosis should have been established by any and all means including an exploratory operation at that time.

At the age of 15 years, this patient was found to be genetically a male, endocrinologically a castrate, but psychologically more female than male, and, because of "the intellectual inadequacy, inflexible attitude, overdetermination and exaggeration of feminine behavior, the psychologic pattern of adamant insistence that she remain a girl, there seems to be no other alternative but that we accede to her wishes." (M. B.) Had this situation not been predetermined by early conditioning, she could, with relative ease, have been treated endocrinologically and surgically to develop male characteristics.

The marked growth of breast tissue in this patient indicates that certain genetic males have the potentiality for the development of breast tissue when properly stimulated. We know from past experience that this cannot be done with all men, but the significance of this observation is not clear. Very likely it is on a genetic basis and dependent upon the amount of glandular tissue present at birth. An analogous situation is found in certain small-breasted women who are perfectly normal hormonally, but who have inadequate mammary tissue.

It is of interest that, 12 months after the creation of a vaginal canal and the implantation of estrogen pellets, the "clitoris" still remains the sole locus of genital, sexual excitation. Whether this tract will ever become an erotogenic area is not known. The interruption of nervous pathways incident to the surgery may, of course, prevent this. The absence of such a development in this patient may have no meaning, but the transformation of this artificially created vagina into a primary zone would have real psychologic implication.

The importance of early rearing influences in the determination of adult sexuality is well illustrated by this patient, who, after having plastic surgery performed so that her physical and psychologic identities were similar, was able to make a fairly good social and emotional adjustment, whereas previously the conflict between physical maleness and psychologic femaleness had been intolerable. This original conflict is not unlike that seen in the usual type of male homosexual. Certainly the history of this patient, as well as others who have been described in the literature, should convince even the most conservative of physicians that congenital factors are relatively unimportant in the determination of psychosexuality. Emphasis must be placed where it belongs: on the early training of the child, and the treatment of abnormalities in psychosexual development is the province of the trained psychiatrist. The endocrinologist and surgeon may often be of help in correcting physical deviations, but in the hands of the psychiatrist rests the correction of the psychologic difficulties.

In retrospect, it is the opinion of the authors that this patient may have been poorly managed. The psychiatrist feels that K.'s behavior is characterized not so much by femaleness as by a violent suppression of maleness and believes that there may well be a failure of femaleness eventually. The correct diagnosis should have been established by surgical exploration in infancy and corrective procedures instituted soon thereafter. Endocrine influences become manifest only at, or shortly before, puberty, so that hormonal studies are of no help before this time. Faced with the problem of this 15 year old male patient who was determined that female characteristics must be developed, it may be that the present authors had no choice but to proceed as they did. However, the ultimate psychologic prognosis for this patient is in doubt.

SUMMARY

The case of K. R., a 15 year old male pseudohermaphrodite, is presented. After careful psychologic evaluation by a psychiatrist and social worker and intensive study by an endocrinologist, plastic surgery and endocrine treatment were instituted in order to promote development of female sexual characteristics so that the patient might live as a woman. The reasons for this decision, as well as certain theoretical considerations, are discussed. It is considered that the prognosis for eventual adjustment to femaleness is likely to be poor. A plea is made for early correct diagnosis in patients of this type, with corrective procedures instituted at as early an age as possible in order to minimize the trauma to the development of a relatively normal psychosexual personality.

The authors thank Drs. William Stoner and Edward Henderson of Schering Corporation for the estradiol (PROGYNON®) pellets used in this study.

CLINICAL STUDY

Stigmonene Bromide in the Management of Postoperative Distention

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By means of gentle stimulation of the gastrointestinal tract, STIGMONENE BROMIDE,** *a new and comparatively nontoxic synthetic parasympathomimetic, was found effective in both preventing and eliminating abdominal distention due to (postoperative) intestinal atony in the majority of 100 major surgical cases.*

SURGICAL procedures carried out in the pelvic or the abdominal cavity of necessity are accompanied by trauma of varying degrees. The trauma may be so mild that it causes no clinical manifestations. On the other hand, especially following extensive and prolonged surgery, the trauma may be so marked that it causes postoperative shock. The trauma, of whatever degree, affects the autonomic nervous system and is one of the major causative factors in autonomic imbalance. When this imbalance is sufficiently pronounced to result in clinical manifestations, it poses the problem of treating abdominal distention as well as facilitating recovery from operation.

Modern surgical technics and equipment and present day methods of patient management have helped greatly to reduce postoperative complications such as intestinal atony, abdominal distention, urinary bladder atony and urinary retention. Nevertheless, these complications are still sufficiently high in incidence and severity that they constitute disturbing and, at times, even dangerous states which must be overcome.

Apparently the trauma attendant upon surgical intervention disturbs the physiologic acetylcholine/cholinesterase balance, which is an important factor in the autonomic imbalance. It has been established experimentally that acetylcholine is the physiologic chemical mediator of the parasympathetic postganglionic, autonomic preganglionic and motor nerve impulses.[1] Whitaker and Wright emphasize its importance, stating that "acetylcholine is not only produced at the neuromuscular junction of the parasympathetic nerves but also at the synapses in the ganglia of this system."[2]

In recent years many investigators—Loew and Navratil (1926), Plattner and Hinter (1930), Englehart and Loew (1930), Feldberg (1933), Schweitzer, Stedman and Wright (1939)—have shown that the parasympathomimetic or cholinergic effects of acetylcholine can be prolonged and intensified by inhibiting or delaying its enzymatic hydrolysis by cholinesterase. The cholinergic or physostigmine-like drugs are capable of bringing about these same effects. However, the toxicity or undesirable side reactions of most of these drugs impair, to a surprisingly large extent, their clinical usefulness.

A cholinergic drug which is effective and, at the same time, of low toxicity is of great potential therapeutic value. Its clinical use should reduce the incidence and severity of abdominal distention and urinary retention or eliminate entirely these postoperative complications. With these considerations in mind, the new synthetic

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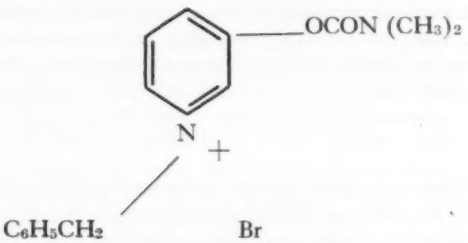
**STIGMONENE BROMIDE® was made available by William R. Warner & Co., Inc., New York, New York.

cholinergic drug, STIGMONENE BROMIDE®, was subjected to clinical evaluation.

Stigmonene bromide is a synthetic, alkaloid-like salt of the quarternary pyridinium series. Quantitatively, it appears to display longer-lasting physiologic and pharmacologic actions than other physostigmine-like drugs. The drug's effectiveness as a parasympathomimetic or cholinergic stimulant through inhibition of cholinesterase has been established in pharmacologic and animal experimentation.[3,4]

Stigmonene was utilized in this study in 1-cc. ampules of a 1:2000 solution (0.5 mg.) of the bromide salt. Empirically, the formula of the drug is $C_{15}H_{17}BrN_2O_2$. Chemically it is 1-benzyl-3-(dimethylcarbamyloxy)-pyridinium bromide. The structural formula is as follows:



The drug is stable and is soluble in water and alcohol.

It was decided to use stigmonene bromide in 100 cases of major surgical procedures, i.e., abdominal, gynecologic and urologic operations (Table 1). Both men and women were included in the series and the patients ranged in age from 12 to 74 years.

TABLE 1

STIGMONENE BROMIDE IN MAJOR SURGERY

OPERATIONS	NUMBER OF CASES
Abdominal	88
Cholecystectomy	19
Cholecystectomy and hepatic cystectomy	1
Cholecystogastrostomy	1
Cholecystostomy	1
Appendectomy	20
Appendectomy and drainage	2
Appendectomy and resection of ovarian cyst	1
Herniorrhaphy	23
Gastric resection	4
Closure of perforated peptic ulcer	1
Resection of colon (sigmoid)	1
Ileostomy	1
Sigmoidostomy	1
Exploratory laparotomy	1
Exploratory laparotomy, lysis of adhesions	4
Exploratory laparotomy, incision and drainage of retroperitoneal abscess	1
Exploratory laparotomy, closure of perforated gastric ulcer	1
Exploratory laparotomy, biopsy of stomach	1
Exploratory laparotomy, gastroenterostomy	1
Exploratory laparotomy with drainage of common duct	1
Excision of retroperitoneal leiomyosarcoma	1
Release of intestinal obstruction	1
Gynecologic	10
Salpingo-oophorectomy	4
Hysterectomy, salpingo-oophorectomy	1
Hysterectomy, salpingo-oophorectomy and appendectomy	4
Resection of ovarian cysts	1
Urologic	2
Cystectomy	1
Nephrectomy	1
TOTAL	100

THE recommended dosage of stigmonene bromide is 1 cc. of a 1:2000 solution (0.5 mg.) administered by intramuscular injection, repeated every three to four hours until a total of not less than six injections has been given. In conducting this evaluation, it was decided to give additional injections (over and above the recommended total of six) if and when necessary.

When the drug was administered *prophylactically*, the first dose of 0.5 mg. was usually injected immediately upon conclusion of the operation and this dose was repeated every four hours until either six intramuscular injections had been given or the re-establishment of normal intestinal tonus was clinically evident. When the drug was administered *therapeutically*, namely as a treatment for established or fully developed distention, the dose of 0.5 mg. was injected intramuscularly every three hours until the distention disappeared.

The minimum number of intramuscular injections in any case was that which is recommended, i.e., six injections of 1 cc. of the 1:2000 solution (0.5 mg.). However, one patient received 49 consecutive intramuscular injections (1 cc. of the 1:2000 solution at four hour intervals) without ill effects. In no instance did stigmonene have to be discontinued because of side effects or toxic symptoms.

Stigmonene was used prophylactically in 76 surgical cases. Of this group 40 patients had uneventful and uncomplicated postoperative courses; only 23 patients developed mild distention. Mild distention is defined as the patient's state when the abdomen becomes even slightly tympanitic to percussion but the postoperative course is otherwise uneventful. In other words, of the total group of 76 cases, 63

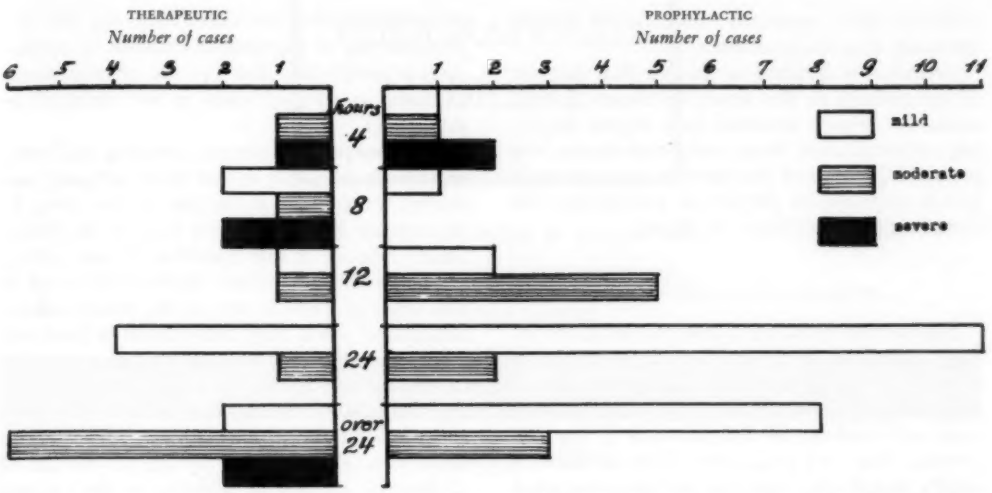


FIGURE 1. Incidence and time distribution of abdominal distention following postoperative use of stigmonene bromide in 100 cases.

patients (82.9 per cent) presented no great problem and made excellent postoperative recoveries.

With respect to the remainder of the 76 cases in which stigmonene was used prophylactically, 11 patients developed moderate distention and 2 developed severe distention. Both moderate distention and severe distention refer to intestinal atony with abdominal distention which is objectively evident and which causes subjective distress to the patient. Only 13 patients (17.1 per cent) of the group in which stigmonene was used prophylactically developed abdominal distention of a clinically significant degree.

Stigmonene was used therapeutically in 24 cases of established or fully developed abdominal distention—i.e., the drug was not administered until after the disorder was evident. There were 9 patients with mild distention, 10 with moderate distention and 5 with severe distention. After institution of stigmonene therapy, the patients experienced subjective relief very early in the course of injections. Advancement of the intestinal atony and the accompanying distention were promptly arrested and progressive regression in the distention occurred within a few hours and continued without interruption until recovery.

Of the group which developed mild distention (9 patients), the disorder remitted and the atonia disappeared in less than 24 hours in 7, and in only 2 patients did symptoms persist for slightly more than 24 hours. In the 10 cases with moderate distention, relief was obtained in less than 24 hours in 4 cases and in slightly more than 24 hours in 6 cases. In the 5 cases with severe distention, relief of all symptoms was obtained in less than 24 hours in 3 cases and in a little more than 24 hours in 2 cases.

THE results obtained from both the prophylactic and the therapeutic use of stigmonene are shown in Figure 1. It is evident from study of this figure that the prophylactic use of stigmonene in this series of surgical cases, in which the regimen of early rising was also applied, offers the surgeon and the patient the most gratifying results.

If it is elected to omit the important precautionary measure of employing prophylactically a cholinergic stimulant in surgical cases, it is also evident from Figure 1 that the postoperative distention which may develop can be effectively curbed within 24 hours in the majority of cases. While it is comforting to know that an effective remedial agent is available for the correction of this abdominal distention, on the basis of these findings the prophylactic use of stigmonene is deemed preferable and is highly recommended.

It should be mentioned that the Levin tube with suction was employed in 8 of the 100 cases in this series, in accord with the practice of

utilizing such apparatus routinely in gastrointestinal surgical procedures.

Attention is directed to the fact that not one of the patients in this series developed bladder atonia or urinary retention to a degree requiring catheterization. Since early ambulation was practiced by most of the patients, the exact role which stigmonene played in preventing this complication is difficult to define.

SUMMARY AND CONCLUSIONS

Stigmonene bromide, a new synthetic cholinergic stimulant, has been clinically evaluated in a series of 100 patients who underwent major surgical operations. On the basis of the observations and findings in this series, it is our impression that: (1) stigmonene bromide exerts a mildly stimulating effect on the gastrointestinal tract which can prevent or eliminate intestinal atony and abdominal distention; (2) the prophylactic use of stigmonene bromide in surgical cases is preferable, and (3) use of stigmonene bromide in surgical cases is not attended by side effects.

The postoperative nausea, vomiting and sweating which did occur in this series were not necessarily attributable to the use of this drug. In no instance did stigmonene have to be discontinued because of side reactions or toxic effects.

The absence of urinary retention observed in this series of cases is one of the results usually anticipated when early ambulation is practiced. The concomitant absence of any manifestation of urinary bladder atonia—e.g., slowness in starting the urinary stream, less force (lower pressure) behind the urinary stream, and sluggish sphincteric closing—may be due to the use of cholinergic therapy in addition to the practice of early ambulation.

REFERENCES

1. Koppanyi, T.: Acetylcholine as a pharmacological agent. Bull. Johns Hopkins Hosp. 83:532 (December) 1948.
2. Whitaker, J. C. and Wright, L. T.: Abdominal distention. New York State J. Med. 50:437 (February 15) 1950.
3. Sakal, E. H.: The search for therapeutically useful parasympathomimetic compounds. Journal-Lancet 70:474 (December) 1950.
4. Schachter, R. J., Ercoli, N., Chessin, M. and Wurst, H. M.: The pharmacologic properties of a group of cholinergic compounds with a pyridinium nucleus. (To be published.)

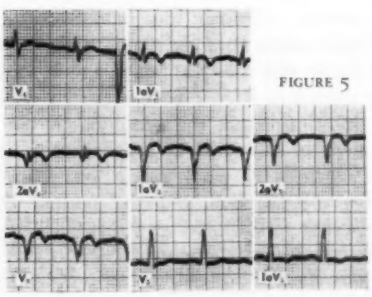


FIGURE 5

CORRECTION

In mounting Figure 5 of the article, "Herniated cervical intervertebral disk simulating angina pectoris," by Weinberg et al. in the September issue (page 252), portions of the electrocardiogram were labeled incorrectly and reversed. The corrected figure is reproduced here.

POSTGRADUATE MEDICINE

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EDITORIALS

OCTOBER 1951

SUDDEN DEATH DURING SEXUAL INTERCOURSE

Because of its dramatic implications, a certain amount of folklore and literature has accumulated around the subject of sudden death during sexual intercourse, be it as part of a novel by Scholem Asch, a short story in the *New Yorker,* or such rumors as were circulated in the town where I spent my younger years, which boasted that its famous red-light district was responsible for the end of two reigning monarchs of Europe.

The *Index Medicus* does not show any paper on the subject since 1927; nevertheless, these cases are not too uncommon. At a recent meeting of the American Academy of Forensic Sciences, numerous participants mentioned such cases from their own experience. From the pathologic standpoint, the mechanisms of deaths involved are essentially the same as those found in sudden deaths in general. Some of the specific problems involved are due to the fact that such a death will frequently produce an embarrassing social situation. A physician who is first at the scene of such an accident will be wise to remember all the general rules that apply to the investigation of sudden and unexplained deaths.

To recapitulate briefly, the most important of these are as follows: If a physician has definitely established that death has occurred, he should keep away all unauthorized personnel and see that the position of the body and the surrounding articles are disturbed as little as possible. He should see that the body is not moved before the police have arrived and have taken pictures and gathered all other information they desire.

Frequently, the female partner (with one exception to be mentioned later, all the deaths known to me have occurred in males) may have left in a panic and only indirect proof of sexual activities may be obtained, such as identification of seminal stains. It also may be helpful to wash the penis with saline solution, centrifuge this fluid, and sometimes it is possible to demonstrate vaginal epithelial cells in this centrifuged specimen.

Some of the problems involved are demonstrated by the following case report:

I was called by the coroner of a neighboring county to investigate a death. At the time I was called, the body had already been moved to an undertaking parlor. From the coroner and the chief of police, the following history was obtained: The deceased, a 65 year old white male, was found at 9:00 o'clock in the morning by his landlady. The body was unclothed, lying on its back, and some smudges of lipstick were noticed on the face. There were some stains on

the sheets, which were identified by the police as seminal stains. It was established later that he had had female company during the night and the companion was apprehended. She stated that they had a long-standing liaison, that he had been in good health and free of complaints, and that he suddenly collapsed during intercourse. She (being a married woman) had become panicky and left immediately. However, this being a small town, she was found rather quickly.

Autopsy revealed the following findings:

External description: This is the body of an elderly, obese white male, measuring approximately 170 cm. in length and weighing approximately 85 kg. Marked rigor mortis is present and marked lividity on the dependent parts. The pupils are round and equal. The lips are not cyanotic. Smudges of lipstick are seen on the upper lip. There are no signs of external injury.

Internal description: The midline fat measures 2 cm. in thickness. The peritoneum is smooth and glistening. Both pleural cavities are completely free of fluid, blood and adhesions. The pericardial sac is smooth and glistening on the outside. It is markedly distended so that the apex is at the level of the seventh rib about 13 cm. to the left of the midline. The left lower lobe of the lung is pushed upward by the pericardial sac and the latter has a dark blue transparent appearance. Upon opening the pericardial sac one encounters between 500 and 1000 cc. of partially clotted blood.

Body organs: Heart: The heart is of average size and covered with a few petechial hemorrhages posteriorly. A perforation is present in the posterior wall of the right ventricle near the septum and near the coronary sulcus. Upon opening the heart, the endocardium is smooth and glistening except posteriorly near the septum. The myocardium is reddish brown and firm except in the same posterior region. In this posterior region, surrounding the perforation, the myocardium is extremely soft and friable for a territory which is about 6 cm. in length and perhaps 2 cm. in width. On sectioning, it is dark red, mottled with yellowish areas and the muscular pattern is lost. The coronary arteries are sclerotic and narrow and no coronary supply can be traced to the necrotic area described above. The remaining organs do not show any significant gross abnormalities except for marked passive hyperemia.

Microscopic examination: Heart: In the area of softening mentioned in the gross description, the myocardial fibers have lost much of their staining qualities and have broken down. Many segmented granulocytes are seen in the spaces between the myocardial fibers. There is a peripheral area of old scarring and a fresh thrombus in a smaller coronary branch. Lungs: No significant histopathologic changes. The spleen shows marked passive hyperemia. Liver and kidneys: No significant histopathologic changes.

Anatomic diagnosis: (1) Recent infarction of posterior wall of right ventricle (approximately 48 hours duration). (2) Rupture of posterior wall of right ventricle. (3) Hemopericardium.

Comment: Sudden death due to coronary disease represents one of the most common mechanisms of death. The unusual feature was not only that death occurred without any premonition—this occurs fairly often in coronary disease—but that no symptoms were present, although a myocardial infarction had occurred at least 24 hours earlier. The mechanism in this case is fairly easily understandable. The infarcted area was comparatively small in size and did not reduce significantly the quantity of functioning myocardium. Unfortunately, the infarction was located in the posterior wall, which means it was located in the region of the myocardium which is farthest away from the coronary ostia and here the chances of major collateral circulation are the worst. Therefore, in a limited area, a complete necrosis of the entire wall of the right ventricle took place, thus producing a spot which could easily perforate under increased physical and cardiac activity.

To digress a moment, it has been my repeated experience that a fairly small posterior wall infarct can be quite deadly. Another example is that of a railroad worker who had slight indigestion during one evening and collapsed the next day, dying within an hour. Here, the complete necrosis, so common in posterior wall infarction, had affected the posterior papillary muscle of the mitral valve which had ruptured and thus produced nearly instant death.

Another mechanism of death during intercourse is one that affects a somewhat younger age group. Here, on autopsy, a con-

genital aneurysm is found somewhere in the circle of Willis and rupture of such an aneurysm, as we all well know, can produce death with great rapidity. As far as I have been able to ascertain, all the deaths reported have occurred in the male, except in one case mentioned at the recent meeting of the American Academy of Forensic Sciences. In this instance, a young couple checked into a hotel for their honeymoon and, a few hours later, a physician was called to find the bride lying dead in bed in a pool of blood. Careful autopsy revealed a torn hymen which connected with a large plexus of veins at the posterior wall of the vagina, obviously a malformation, and a fatal hemorrhage had ensued.

It is also appropriate to give some considerations to the psychogenic factors involved. As mentioned before, a certain number of these deaths occur outside of home and represent illicit intercourse. Furthermore, they seem to occur with greater prevalence among males of somewhat advanced age where such factors as fear of discovery, embarrassment and worry about potency may have a certain influence. At the Academy meeting, one of the participants mentioned a group of three fairly young brothers each of whom died the first time that intercourse was attempted. Unfortunately, we have no autopsy reports.

While not actually due to structural disease, a certain group of fatalities should be mentioned here in which joint deaths during intercourse are reported from various sources. This group of deaths represents a typical complication of our modern civilization and of the automobile which is well known not only as certain means of transportation, but also as a man's castle and frequently the only place where a couple can have a certain amount of privacy. Not too infrequently, couples are found in parked automobiles usually with the gasoline tank empty and the ignition switched on. These are cases of carbon monoxide poisoning.

FREDERICK P. BORNSTEIN
Pathologist, Herrin (Illinois) Hospital

SECOND INTERNATIONAL POLIOMYELITIS CONGRESS

More than 500 delegates from 39 nations attended the Second International Poliomyelitis Congress, held in Copenhagen, Denmark, September 3 to 8. The program had been most carefully arranged through a series of committee sessions that began in 1949. The reviews included a recapitulation of our existing knowledge of the disease as far as concerned the virus, epidemiology, prevention, pathology of the nervous system, diagnosis and treatment. Another special session was devoted to psychology and problems of rehabilitation.

Never before have as many distinguished investigators of a single disease been assembled in one place to exchange information concerning recent advances and to plot the plan of attack for the years to come. Optimism may be expressed as to the hope for a diagnostic test, a preventive vaccine, the use of human gamma globulin as a preventive substance, and the eventual development of an antibiotic which will specifically affect the virus of poliomyelitis.

From time to time some have urged that the organization of groups for attacks on individual diseases is perhaps economically unsound and perhaps wasteful. This attack has been made particularly against the organizations associated with such diseases as poliomyelitis and multiple sclerosis, somewhat less against epilepsy, and perhaps not at all against organizations to attack cancer or tuberculosis. Nevertheless the record of progress of knowledge against poliomyelitis that becomes apparent when one compares what is known today with the amount of information that was available only 10 years ago should indicate to any competent observer that an intensive, well supported attack on a single disease pays vast dividends.

A new aspect of the current assembly is the usefulness of such a gathering for the advancement of international peace and understanding. The representatives of 39 different nations were entertained at beautiful

cocktail parties and dinners by officials and by representative Danish organizations. Among these, the reception by the American ambassador Mrs. Eugenie Anderson and her husband, the dinners by Professor Ørskov, head of the State Serum Institute, and by Professor Niels Bohr, one of the greatest of the citizens of Denmark, should be given special mention. The number attending the receptions given by the Danish Medical Association and the Danish Foundation for Infantile Paralysis were so great that it was necessary to stagger the attendance over a period of three hours. This reception was held in the beautiful home of the Danish Medical Association, developed since the end of the war, because the home previously occupied had been bombed by Nazis during the war period.

At one dinner party two of the greatest virus experts from Great Britain, notably Professors Andrewes and Anderson, two Danish investigators, two American investigators, two Swedish investigators, a Frenchman and a Finn were present and the social relationship did much not only to cement friendship but also to permit the development of future visits from one country to another, making possible the firsthand observation which plays a large part in intensifying the speed of progress.

The opening session was attended by the Queen of Denmark, who is a patroness of this Congress, and included addresses by President Hansen of the University of Copenhagen, Niels Bohr and Mr. Basil O'Connor. The address of President Hansen emphasized the importance of developing young men who will carry forward the research of the present into the progress of the future. He emphasized also the great gains that had come from exchange fellowships between the European nations and those of the Americas. Professor Bohr indicated that the knowledge of the basic sciences which is now being applied in the field of biology is having tremendous effects and he felt indeed that the application of the methods of physics to the study of biologic phenomena might yield results which would extend even into the field of understanding of the human psyche. Mr. O'Connor presented the gavel of the First International Congress in the name of Franklin Delano Roosevelt whose spirit and initiative had made possible the organization of the National Foundation for Infantile Paralysis and also the International Poliomyelitis Congress.

One needs only to review the program of this congress to understand how great a part has been played by the investigators of the United States in the advancement of our knowledge. More than 80 per cent of all the contributions had been made by American investigators and fortunately this was accepted by the European scientists not in any spirit of dissatisfaction but rather as setting a pattern for methods of attack on unknown fields in medical science. The American investigators were made most welcome and through their visits to the hospitals, the university and the great Serum Institute they themselves received inspiration and suggestions for further research.

The numerous papers and discussions as well as the significant pronouncements of President Hansen and Niels Bohr are to be published in a book in the near future and will be made available throughout the world. The book which represented the progress of the First International Poliomyelitis Congress was published within a few months after that congress ended and already almost 10,000 copies have been circulated throughout the world. In this way the benefits of this great occasion will be extended and will mean immense good for people everywhere.

MORRIS FISHBEIN

BRAIN INJURIES ATTRIBUTABLE TO BOXING

Since television has brought boxing, both amateur and professional, into the sitting rooms of many homes, people are becoming more and more aware that this sport carries with it hazards greater than

those of any other form of physical activity.

Deaths from boxing are not frequent in relation to the great numbers who box. When they occur, they may be due to hemorrhages into the brain from the bursting of blood vessels or, as occasionally occurs, from the bursting of a cerebral aneurysm. Rarely does death occur from a fracture. Occasionally sudden death is associated with a disability of the heart that has not been recognized.

MOST common of the hazards inherent in boxing is the condition called "punch drunk." A boxer receives a blow on the point of the jaw and as a result becomes unconscious. The brain undergoes a condition that has been referred to as commotio cerebri. According to present concepts, the force extends through the jawbone and temple bone to the balance organ of the inner ear and reflexly to the brain. A less powerful blow may fail to produce unconsciousness but can produce a dimming of consciousness so that the fighter's movements become uncertain and he fights on as if dazed. This disturbance of consciousness lasts but a few seconds after which consciousness is normal but the boxer does not remember what happened.

The subject has recently been reviewed by Dr. Sole Raevuori-Nallinmaa, a Finnish physician. He indicates that repeated groggy states of the type described end with permanent effects on the mind and nervous system of the boxer, producing eventually a state of traumatic dementia which is a scientific term for punch drunkenness. Records indicate such psychic changes in 60 per cent of professional boxers who have fought at least five years and at least 5 per cent reach the stage of complete punch drunkenness.

The clinical picture as described by the Finnish physician is sharply delineated. The boxer boasts of being in good condition and underestimates his opponents. He shows disturbances of coordination of thought and his reactions become slow. His memory deteriorates as do also his concentration and attention. Often in conversation, those who are punch drunk repeat themselves. They may even appear at times to be intoxicated, with glassy and staring eyes, indistinct speech and tottering gait. Repeated severe headaches, buzzing in the ears and dizziness may come on with the early stages of punch drunkenness and later disappear.

From a scientific point of view, Cruz has described three aspects of punch drunkenness, including psychic, extrapyramidal and pyramidal. The extrapyramidal form resembles parkinsonism with tremor and other parkinsonian symptoms. In the pyramidal form spastic paraplegia, hypertonia, general anesthesia, decrease of the mobility of the legs, acceleration of reflexes, but seldom any disturbance of the arm, are seen.

Most of the evidence coming from pathology indicates that multiple small hemorrhages occur in the deeper regions of the brain, especially the corpus striatum and these areas are surrounded by degeneration. As the changes develop, the boxer does not tolerate blows on the head easily and every blow is likely to have more permanent effects. The boxer becomes unconscious more easily and begins to lose repeatedly.

As with other physical disturbances known to scientific medicine, "punch drunk" can be prevented by avoiding boxing. The tendency at present seems to be toward more and more boxing; the financial rewards are great for success. Television has made the excitement of combat known not only to boxing fanciers but also to anyone who can have access to a television machine.

MORRIS FISHBEIN

Men of Medicine

"...the World will make a Beaten Path to Your Door"

Every once in a while undergraduates show a surprisingly accurate understanding of the capabilities of their fellow students.

The fellow students of Dr. O. H. Perry Pepper displayed unusual insight in the issue of *'Scope* put out by the University of Pennsylvania Medical School's class of 1908. It said of him: "Our acquaintance with Perry has shown him to be one of the best. His evident determination to make good, his own efforts being the 'exciting cause,' rather than to depend upon certain 'predisposing causes' to make his future secure, is the sort of thing that wins out in the long run. For this reason we expect to hear great things of Perry. Here's hoping."

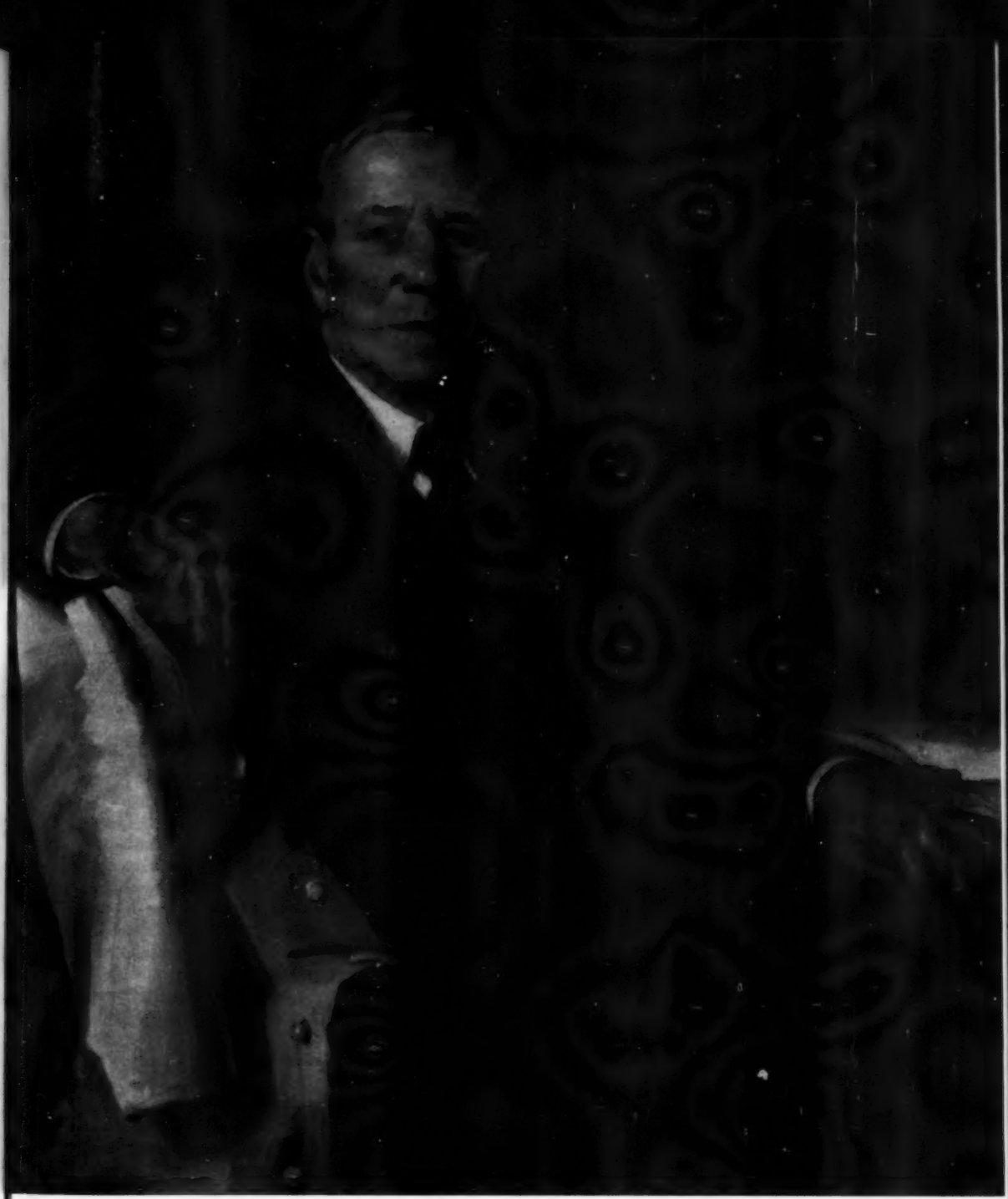
Then, in a section coyly called "Differential Diagnoses," the *'Scope* named Perry Pepper first among the three it thought would make "the most successful physician."

Dr. Pepper, who became professor of medicine emeritus at the University of Pennsylvania Medical School in July, has indeed become a most successful physician and teacher of physicians. He is known and beloved by two generations of physicians he has taught and, at 67, looks forward to many more years of teaching in spite of the *emeritus* at the end of his title. The Pepper influence has pervaded Penn's medical school in Philadelphia and has helped make it the famous school that it is.

There are other hints in the medical school yearbook for 1908 that are helpful in understanding Dr. Perry Pepper and his career in Philadelphia. There is, for one thing, a photograph of a certain statue erected in honor of Dr. William Pepper, provost of the University of Pennsylvania from 1881 to 1894 and professor of medicine from 1884 to 1898, and for whom the William Pepper Medical Society was named. It was Dr. William Pepper—young Perry's father—who conceived the idea of building the University of Pennsylvania Hospital, the first ever owned and operated by a university for the purpose of teaching medicine. Years later, as an undergraduate, young Perry Pepper was to be president of the society named for his father, and not only to study but also to teach at the very hospital which his father had been instrumental in founding. His grandfather, also Dr. William Pepper, was also professor of medicine at the University Medical School, from 1860 to 1864—quite a few years before grandson Perry became the first president of the Undergraduate Medical Association. . . . There was a third Dr. William Pepper too: Perry's older brother, who was named assistant professor of clinical pathology in 1907 and who became dean of the Medical School in 1912.

Obviously, there were many "predisposing causes" for Perry Pepper's success, but he was able to grow to such professional stature that it was never said of him: "Oh yes, Dr. Pepper's grandson," or "Oh yes, Dr. Pepper's son," or "Oh yes, Dr. Pepper's brother." Nobody has had any doubt, for many years, as to which of the Doctors Pepper was meant when the name was mentioned. Perry Pepper has made his own way against a formidable family background of famous Philadelphia physicians and has achieved his own identity. Now, 43 years after graduation, Dr. Pepper is at the peak of his powers, vitally interested in medicine and in the teaching of medicine. His interests range from geriatrics to writing delightful verses for children. Modest, and apt to underestimate the importance of his own career in Philadelphia, Dr. Pepper has developed into a physician-philosopher whose medical writing portrays much of his personal charm.

Still another item in the pages of the yellowing 1908 yearbook is an advertisement for a spring water. Its selling point was: "Avoid Typhoid Fever by Using a Sanitary Water." . . . "There is not much typhoid around now," said Dr. Perry Pepper, thinking back to those days and taking off the tortoise shell glasses which



O. H. PERRY PEPPER, M.D.

Portrait by John C. Johans (1947), hanging in the University of Pennsylvania Medical School.

he uses only for reading. "We did have a case of typhoid here last year. It felt like old times." There was a trace of regret in his tone as he thought back to the days when doctors had to combat typhoid epidemics, but his gray eyes twinkled as he said: "They keep an old guy like me around for the old view. Why, these young fellows have never seen cases of typhoid, or smallpox, or empyema following pneumonia. They need some old fellow like me to tell them!"

It took a good deal of courage for Dr. Perry Pepper to start practicing medicine in Philadelphia, where the Pepper name was so well known. His full name added lustre in Philadelphia too; Oliver Hazard Perry Pepper. He was named for Commodore Oliver Hazard Perry, remembered for his succinct message after the Battle of Lake Erie during the War of 1812: "We have met the enemy and they are ours." He is descended from Commodore Perry through his mother's side of the family, and also from Philadelphia's hero, Benjamin Franklin; he is, as a matter of fact, Franklin's great-great-great-grandson. Dr. Perry Pepper does little to remind anyone of his ancestors. Mementos of Commodore Perry can be seen in his rambling two-story stone house at Ithan, on Philadelphia's Main Line, but a visitor has to remark about the painting of Commodore Perry, a model of his ship or the pile of cannonballs used in the battle before being told why they are there.

Indeed, Dr. Perry Pepper had thought of practicing somewhere else. But he stayed on in Philadelphia because of the illness of his mother. He has never studied abroad, nor has he taught or practiced anywhere but Philadelphia.

He has felt conscious of a certain "ingrownness" because, following graduation in 1908, he walked into University Hospital as an intern and has been there ever since. But nobody else has ever been conscious of any ingrownness in Perry Pepper as he has reached out for new things—new ways of treating patients, new ways of teaching physicians.

In order to overcome Philadelphian "medical provincialism," Dr. Pepper has been conscientious about attending medical meetings, visiting other medical schools and teaching hospitals, and in taking a leading part in medical societies. Now he attends only the medical meetings in which he is most interested, including those of the Association of American Physicians. During the school term he has three teaching periods a week and one clinic at University Hospital. The clinic, for third and fourth year men, consists of "the most interesting cases in the hospital," without regard to any specialty. It may be a "little conceited" to ignore specialties in these days of specialization, he says, but finds that his clinics help the students' general understanding of medicine. During the school year, too, he makes his hospital rounds.

Still wearing a long white coat, Dr. Pepper is in his office every week day, even in summer, except when out of town on vacation. But he does not come in on Saturdays and Sundays; he did that for 25 years, he says, and "that's enough."

On his desk in the Maloney Pavilion of the University Hospital is a lamp made from the brass rail of the amphitheater of the old medical building, torn down last year. On it is the inscription: "Made from the brass rail of the amphitheater where you taught us all—Perry Pepper from his staff." The lamp itself was made by a patient.

That is the kind of tribute Dr. Pepper appreciates. He thinks less of some of the formal tributes he is receiving on the occasion of his nominal retirement. The honors that please him most are those from medical societies—especially from the Association of American Physicians, that group of the medically elect, of which he is a former president. But he likes to think of them as tributes not so much to himself, as to his medical way of life—as he says, "My career demonstrates an appreciation of clinical medicine. I like to think of the honors I have received as honors for someone who has never done anything outstanding in research, who stands for almost nothing except teaching and clinical medicine." And it is clinical medicine which has become the hallmark of the University of Pennsylvania Medical School.

Dr. Pepper, and the University of Pennsylvania Medical School, have always stood for emphasis on turning out high grade practitioners and never letting research spoil teaching or the care of the patient. He looks at research in a teaching hospital as essential but not the only goal. Nowadays, Dr. Pepper believes, there is too little thoughtful diagnosis, too much reliance on laboratory tests and too much indiscriminate use of antibiotics.

To make this point clear, he tells of a new-style clinic he claims he has just heard about. The patient enters through a revolving door. At one turn of the door he is x-rayed, at another some blood is taken for tests. At the last turn, he is given an injection of 1,000,000 units of penicillin, and then put to bed. If he is not better in three days, the doctors at the mythical clinic ask him his symptoms.

So, all through his teaching career, Dr. Pepper has been stressing the need for a careful physical examination of the patient himself—not merely a study of his laboratory tests—and a thoughtful taking of his case history, no matter how much time the two procedures take.

This does not mean that Perry Pepper has no use for modern technics, or that he has an unbounded admiration for the old-time doctor who diagnosed so often by hunches. He believes in using modern tests, but not in letting them take over the medical show; he is suspicious of some of the reported "instinctive" diagnoses by pre-x-ray clinicians. There were, he points out, no x-ray or laboratory tests made to confirm the flash diagnosis, and usually no autopsy to disprove it.

"Naturally, it does not take much time to diagnose dyspepsia by a look at the tongue or to recognize tuberculosis of the lungs by the expression on the patient's face," he explains. "It would be fine if this was or ever had been possible. Unfortunately, 'dyspepsia' was usually ulcer of the stomach or duodenum, and the x-ray has long since revealed that many cases of so-called phthisis were certainly instances of tumor or abscess or even of pins or peanuts in the lung." It takes time and thought, as well as laboratory tests, Dr. Pepper goes on, to discover that blood in the urine may be due to a food to which the patient is allergic, or that a woman's kidney trouble may be due to a particular kind of shampoo.

One of Dr. Pepper's pioneer contributions to medical teaching was his development of clinics for first year students. Now known as correlation clinics, they are standard practice in almost all medical schools. Dr. Pepper began this innovation in 1922. Penn was the first medical school to have them, Pepper the first professor to conduct them.

He explains now: "I'd go over to the first year classes and find out just what the students were studying in, say, anatomy. Then I'd find a case in the hospital which illustrated the facts they were learning. For instance, suppose the boys had just learned how there could be a referred pain in the shoulder from the gallbladder. I'd show them a patient with gallbladder trouble who complained of a pain in the shoulder. . . . These were the first live patients the students had ever seen. They were tasting blood."

In one of his early papers and in more formal language, Dr. Pepper explained the purpose of the first year clinics: "It is their first taste of the real thing and they are avidly attentive. There is no question that these clinics are enjoyed; they could scarcely be so badly conducted as not to be. . . .

"The student will be convinced from the outset that what he is learning in the courses on anatomy, physiologic chemistry and physiology is actually of practical importance and everyday usefulness to the physician and surgeon. . . . The interest of the students in their work will be stimulated, their appetite for medicine will be stimulated and their curiosity excited."

These Perry Pepper clinics were, one of the first year men recalled many years later, "the best damn' clinics I ever attended."

Dr. Pepper's manner with his students was recalled recently by an associate who had seen him in action, and remembered him as a man inclined to reject the obvious at his clinics and instead to stress the significance of atypical features of a case. Dr. Pepper displayed "a lightning-quick detection of inconsistent or illogical thinking." When students were wrong, he had ready a "sly but devastating thrust, rapier-like but friendly."

ANOTHER bit of Pepper pioneering was done in the field of geriatrics. He was, he believes, the first in the United States to start teaching geriatrics as a separate subject—so long ago that he has forgotten the exact date. The subject matter, of course, had been taught before, but he began to give lectures on geriatrics itself. Now he intends to spend his "old age writing about old age," and has started work on a book on geriatrics. It will be a short book, and to the point. He feels that in discussing pneumonia of the aged there is no use in reporting all the knowledge about pneumonia that can be found in standard textbooks. Instead, he will try to limit his discussion to the aspects of pneumonia that apply to old age—just as a pedi-

atrician should limit his discussion of a disease to the aspects peculiar to childhood.

Dr. Pepper sees many difficulties in the way of understanding the process of disease in the elderly: "It is easy to say that the phenomena of senescence are physiologic and those of senility are pathologic. But this does not help us much because the distinction between senescence and senility is far from clear."

In studying geriatrics, Dr. Pepper has been greatly aided by the twelfth chapter of Ecclesiastes, the chapter that begins: "Remember now thy Creator in the days of thy youth, while the evil days come not, nor the years draw nigh, when thou shalt say, I have no pleasure in them." He enjoys joining in the speculation about the symbolic meaning of some of the passages that have stimulated the imaginations of physicians for hundreds of years. He was especially amused to learn of an explanation of the passage, "and the grasshopper shall be a burden, and desire shall fail." It seems that "grasshopper" is a Talmudic euphemism for the male genital organs.

In his work already published in the field of geriatrics, Dr. Pepper has stressed the idea of returning patients to the "normal of the aged." An old person who is sick cannot expect, on recovery, to have the health he had at 20, but he should expect to have the kind of health a normal old person should have. He makes the point, often overlooked, that the elderly react poorly to medicines but may stand surgery well.

Dr. Pepper was also a pioneer in the use, although not the development, of insulin. He tells about one dramatic case in a paper geriatrically styled *"The long follow-up: a compensation of the aging physician."* It was in 1923, and the parents of a diabetic child were wondering whether it was worth the struggle to try to keep him alive. Said Dr. Pepper: "We decided to continue the struggle, for something might turn up. It did! In March 1923 our patient received his first dose of insulin and his first adequate meal in five years. He was among the first patients to be started on insulin in this city." Later, the boy turned up in Dr. Pepper's medical class at the University of Pennsylvania; he has been on insulin for 28 years.

Then Dr. Perry Pepper expressed the creed of the physician in these eloquent words: "To me this case has given perhaps the greatest satisfaction of any in my medical life, but the credit belongs primarily to his parents. It does not take many such experiences to make a physician glad of his choice of the profession of medicine."

Dr. Pepper has another "first" to his credit. He wrote the first section on virus diseases to appear in a medical textbook—in Dr. John H. Musser's "Internal Medicine," first published in 1932. He had told Dr. Musser that the proposed book should contain such a section, and Dr. Musser told him, "You're hooked." Dr. Pepper protested that he didn't know anything about the subject and Dr. Musser replied that nobody else did, either. So Dr. Pepper followed the advice of Boston's famed Dr. Richard Cabot: "If you don't know anything about a subject, write an article about it." Dr. Pepper wrote the article, and learned a lot about virus diseases "sweating it out for John Musser."

Dr. Pepper's first interest in medicine was hematology, and it was many years before he moved on from hematology to philosophy. He has always tried to avoid having a specialty, but he came pretty close to being a hematologist. It was, Dr. Pepper explains now, a matter of "propinquity, not of love—like falling for the girl who lives in the same block." While he was in medical school, hematology was "the thing to be interested in." It was an active field, closely allied to all clinical problems. Nowadays, as Dr. Pepper points out, it is "through propinquity" that young medical students become interested in the technic of passing catheters into the heart or in the growth of more and more powerful antibiotics.

As a young research scientist, Dr. Perry Pepper made a promising beginning. In the summer of his third year at medical school he worked in the Ayer Laboratory of the Pennsylvania Hospital in Philadelphia with Dr. Warfield Longcope, who was working on his authoritative monograph on Hodgkin's disease.

In connection with this association, Dr. Pepper published his "maiden medical effort," in the *Bulletin* of the Ayer Clinical Laboratory. It was called "A report of a case of Hodgkin's disease with generalized eosinophilia"—the first of 128 papers that Perry Pepper was to write.

This earliest paper had an interesting sequel; months later he received from Sir William Osler a note of praise that enclosed a review of it which appeared in *Lancet*. The note, written from Osler's home at 13 Norham Gardens, Oxford, England, was in longhand. It read:

Dr. Pepper at his desk in his office in the Maloney Pavilion of the Hospital of the University of Pennsylvania.

"Dear Perry. Delighted to see your name—and associated with such a good piece of work. Send me a reprint. It is so nice to see the name kept up so worthily in the third generation. My sincere regards to your mother and to Will." Dr. Pepper still keeps it among his papers.

The review that Osler enclosed was, says Dr. Pepper, so much better than the original article that he is sure that Osler wrote it himself and asked the editor of *Lancet* to publish it. Osler had been associated with Pepper's father during his days at the University of Pennsylvania Medical School. "That was just the sort of thing that Osler did for many young men," Dr. Pepper says now, "and the sort of thing which made him so beloved and so stimulating."

Dr. Pepper was to receive other letters from Osler, including one dated July 14, 1908, in appreciation of his work in the Undergraduate Medical Association. It included a greeting to "Pepper tertius," his brother, William, and closed with an offer to give Perry introductions to prominent medical men in Europe if he should go to the Continent to study—a trip he never made.

Dr. Pepper's interest in hematology continued for many years, and he published many papers on the subject. The titles of these early papers, in contrast with his broader interests of later years, indicate the technical nature of his first steps in medicine. In July 1913 he published, in the *Archives of Internal Medicine,* a paper on "The resistance of reticulated erythrocytes," with Dr. Max M. Peet as collaborator. In 1914 he published in *The Journal of Infectious Diseases* a paper, written with Dr. E. B. Krumbhaar, on "The diminished coagulation of the blood in anaphylactic shock in the dog." In 1915 there appeared in *The Journal of Experimental Medicine* a paper written with Dr. J. Harold Austin on "The relation of the spleen to blood destruction and regeneration to hemolytic jaundice—the importance in the production of hemolytic jaundice of the path of hemoglobin to the liver." He wrote, too, a section on agranulocytic angina for Piersol's "The Cyclopedia of

Medicine." In 1931 he published a paper, filled with fascinating bits of medical detective work, on "A review of the secondary anemias," in *California and Western Medicine*. In 1933 he wrote, with Dr. David L. Farley, the authoritative book, "Practical Hematological Diagnosis."

While he was developing from hematologist to philosopher, Dr. Pepper was passing medical milestones with steady regularity. There were two breaks in the routine of his advancement at the University of Pennsylvania Medical School—the two World Wars.

Born in Philadelphia on April 28, 1884, he attended St. Mark's School in Massachusetts and then entered the University of Pennsylvania, from which he was graduated with the degree of B.S. in 1905. After graduation from the University's medical school in 1908, he interned at the University Hospital for two years. Then, in 1913, he became assistant physician at the hospital. He became assistant instructor in 1911, associate in medicine in 1912, associate in research medicine in 1913, assistant professor of medicine in 1922, professor of clinical medicine in 1928, and, since 1934, professor of medicine.

Actually, World War I meant a change more in scene than in routine. As a lieutenant colonel in the U. S. Army Medical Corps, he was chief of medical service in Base Hospital 69 at Savenay, France. He was, he says now, "in the army, not in the war." Savenay, near Nantes, was far from the front, far from the coast, and he never saw an enemy plane nor heard a gun fired. The center for which he was chief of medicine and consultant had ten 1000-bed hospitals attached to it. He made his rounds just as he would have in Philadelphia. "I was one man in the army," he says, "who got an appropriate assignment."

World War II found Dr. Pepper in a different and more important role, but again he was far from the fighting. He was a member of 17 committees at one time, helping organize the nation's medical facilities for war. This meant spending two or three days a week in Washington and extra work at the hospital and college in Philadelphia, both places short-handed because of the war. Dr. Pepper now says: "I spread myself pretty thin, and I got thin—lost a lot of weight in those years."

The committees on which Dr. Pepper was active make a formidable list. During World War II and postwar periods he was chairman, consultant, referee or member of no less than 21 committees whose responsibilities included everything from medical personnel for Britain to editing the medical section of a history of the war. All this wartime activity Dr. Pepper dismisses as "just committee work," but the truth is that he played a vital part in directing much of this country's medical effort, especially in the field of top-secret biologic warfare.

During World War II, Dr. Pepper delivered a widely-commented-on address called "Escape From War," later printed in *The General Magazine Historical Chronicle* for July 1942. He advised several methods of "escape from the overpowering nerve-wrack of the war-saturated atmosphere in which we live." The most obvious means of escape, he said, was "to lose one's self in one's work." He also prescribed hobbies as a way of building a "bombproof hideout for your psyche."

He described his own hobby—collecting wild mushrooms: "Nowhere will you see signs 'Do not pick the wild fungi.' Two years ago I deliberately decided to find an outdoor hobby. My brother knew too much about birds for me to venture into that field; my wife knew too much about flowers and trees. I wanted something which I could learn about for myself. I chose the wild fungi, or what the uninitiated would call toadstools."

But his enthusiasm for mushroom collecting did not last. It was much too artificial a hobby, and then he read in a book that there were 10,000 common varieties of fungi and became discouraged. He did enjoy painting them, and still paints—out of door scenes, without mushrooms. His wife—the former Eulalia Willcox, whom he married December 2, 1916—paints more professionally, and also does fine bookbinding, an activity that requires unusual manual dexterity as well as artistic ability.

But Dr. Pepper's real hobbies are his practice—and the words used in medicine.

The prescription of losing one's self in one's work, which he recommended in the 1942 wartime paper, he returned to in the paper of last May, "The Long Follow-Up." He said then: "I forgot to mention that in order to watch your patients over many years you must yourself live long. To do so one must maintain a vital interest. Something must make life worth while; and what could be better than the continued observation of the interplay of man and his diseases?"

He still carries on a consulting practice. He regrets having turned down one case recently, a patient who was not in need of emergency care and whose trouble did not seem to offer much difficulty in diagnosis. But she turned out to be a dancer in "Oklahoma!" Dr. Pepper says with regret: "I turned down the wrong patient. Why, I could have got tickets for the show, perhaps gone backstage!"

His experience as a teacher led Dr. Pepper to his interests in medical terms—the tools of his profession—and their etymology. Partly, it was a practical matter. More and more, he found, students were entering medical school without a knowledge of Latin and Greek and so were memorizing medical terms parrot-like, without any realization of their origin. So he began work on his authoritative "Medical Etymology," first published in 1949.

The book, designed to give the student some of the understanding of medical terms he failed to get by not studying Latin and Greek, makes delightful reading. It seasons sound scholarship with sly humor. In the section devoted to dental terminology, Dr. Pepper explains the meaning of "pulp" as derived from the Latin word "pulpa," flesh. Then he adds: "Hence applied to the softer part of a tooth. Cicero used the word pulpa of soft flesh, such as the breasts and buttocks of young girls."

He found an interesting anecdote to explain "carotid," derived from the Greek word "karoun," to put to sleep: "In early Greece mountebanks used to cause goats to fall down motionless by pressure on these arteries and to return to normal by release of the pressure. The great anatomist, John Bell, scoffed at Morgagni for believing this story but, as Leonard Hill recounts in his book on the cerebral circulation, it was later demonstrated that horses and goats depend entirely on the carotids for their cerebral blood supply, since the vertebral arteries in these animals are mere threads where they enter the basilar. So, 'the mountebanks were in the right.' This anatomic condition does not exist in man, but the Spanish word garrote probably comes from this same root, and garrotting does put even a man to sleep."

There is a neoclassic pun in the etymology he gives for the combining form *electro–*. He explains: "All the terms with this root are derived from Gr. *electron* = amber, because amber was the substance in which the phenomenon of electricity was first observed. It would appear that the terminology of everything electric will be Forever Amber."

In tracing the etymology of gonorrhea Dr. Pepper found a fascinating bit of medical history: "Clap, one of the slang names for gonorrhea, dates back to the time of Charlemagne of France, who established houses of prostitution known as *clapiers* or rabbit warrens."

Throughout the book Dr. Pepper has avoided the use of Greek letters. His students, he found, knew just enough of the Greek alphabet to tell their girls what fraternity they belonged to.

Dr. Pepper has lectured, often and amusingly, on the subject of medical etymology. In 1950 he delivered a paper on "Babel in Medicine," before the American Philosophical Society, of which he is a member; the address was later printed in the *Proceedings* of the Society.

As an internist, Dr. Pepper has been interested in the difficult job of defining his own specialty: "An *internist* who is professor of *medicine* in the department of *medicine* in a *medical* school has used what is really the same word four times." Internist, he thinks, is a "terrible word" for it because the internist's interests include the skin as well as the liver.

In 1940 he tackled the problem of the internist in a paper called "What is an Internist?" delivered at the 1940 session of the American College of Physicians. His often quoted definition included such revealing sentences as: "An internist is, of necessity, a physician of exceptional training, for his is the field of greatest width. He must have served his apprenticeship years acquiring information, then slowly transformed that essential but relatively base metal into precious knowledge and, still unsatisfied, devoted his maturer efforts to the transmutation of his knowledge into precious wisdom. . . .

"Being an internist is a state of mind. It implies a breadth of interest which inherently excludes narrow specialism. It demands a vital interest in medicine of the past, of the present, and as far as possible of the future."

It is a hard creed that Dr. Pepper has outlined for the internist, and he has always insisted that the internist live up to his responsibilities. He has never tried to pass the medical buck to the surgeon, for instance, "for the fruitless laparotomy." He likes to turn a worn phrase and point to the internist's blame in cases in

which "the patient lived but the operation was unsuccessful."

The qualifications expected of a man filling the chair of professor of medicine, Dr. Pepper thinks, are not only difficult but impossible. He is asked to be a teacher, a researcher, to have the ability to write and speak in a way to attract favorable attention to the medical school, and to have a large enough private practice to help fill the private rooms in the school's hospital.

"Nobody," Dr. Pepper snorts, "can fill all those requirements." His associates think he has done a remarkable job of fulfilling his own "impossible" conditions, and that somewhere in the etymology of "Pepper" there should be something about doing the impossible.

DR. Pepper's interest in words—and in people—has led him into the exacting field of poetry. Most of his poems he has written for his children: Lalite, now married to Francis A. Lewis, and Oliver H. Perry Pepper, Jr., and for their children. He now has six grandchildren; each of his two children has had three children, two boys and a girl. Neither of his children studied medicine, but there is in Philadelphia a Dr. D. S. Pepper—a nephew, who is assistant medical director of the Penn Mutual Life Insurance Company.

Some of his always delightful poems have a hint of the medical as in "Penicillin"—

Needle and pins, needle and pins,
When a man sickens, his trouble begins.
Into your buttocks and into your thighs,
Nobody cares for your unhappy sighs.

Needle and pins, needle and pins,
I wish I had taken more care of my sins.
Into your veins on the bend of your arm—
Could the disease itself do you more harm?

Needle and pins, needle and pins,
When a man's wicked his trouble begins.
Into the spine 'til the vertebrae break
'Never again' is the promise I make.

Then there is the relentlessly didactic "Teapot Oh Teapot"—

Teapot oh teapot, you're such a nice old thing!
A simple little song to you I think I'll have to sing.
When other folks get mad and hot
They often say things they should not,
But you're so jolly fat and round,
And when you're hot you make no sound,
And when you're boiling, why you only sing!
A cheerful disposition is a valuable thing.

Dr. Pepper has well filled his definition of "the ingenious man"—which he uses in the sense Pepys used it, as meaning a man "possessed of genius."

His memberships in medical organizations indicate his wide interests. He is a member of the A.M.A., member and former president of the Association of American Physicians; member of the American Society for Clinical Investigation, the American College of Physicians (former president); College of Physicians of Philadelphia (former president), and the American Philosophical Society. He was active in organizing the Committee on Certification of Internists, which became the American Board of Internal Medicine and had a large part in bringing about the present high standard of postgraduate training. In addition to his articles in medical journals, he is the author of many "system articles."

This past summer he spent his vacation on Mount Desert Island in Maine—on what he describes as "the unfashionable side," away from Bar Harbor. There, Dr. and Mrs. Pepper have built a group of cabins that look, he reports, like a tourist camp. There are enough of the cabins to house vacationing children and grandchildren, and their dogs.

He hopes to get to work writing his book on geriatrics and preparing a new edition of "Medical Etymology" before long. But the work will not interfere with trips to a nearby golf course. He began to play golf in college, playing on the University's intercollegiate team, and still goes around in the 80's, only about 10 strokes off his college scores.

Dr. Pepper's story has been pretty much that of the University of Pennsylvania Medical School the past 43 years . . . the story of a doctor who stayed in one place all his life and, as it turned out, let the medical world come to him, with the result that young men of the medical world assumed the practice of medicine better men and better physicians for having known him. Like the school, Dr. Pepper expects to go on teaching, and healing, for many more years—in Philadelphia.

GEORGE R. BURNS

New Drugs *and* Instruments

Information published in this department has been supplied by the manufacturers of the products described.

AUREOMYCIN PHARYNGETS*

PURPOSE: Treatment of oral infections.

COMPOSITION: Each orange-flavored lozenge contains 15 mg. of aureomycin hydrochloride crystalline with methylparaben and propylparaben.

INDICATIONS FOR USE: Gram-negative, gram-positive and mixed bacterial infections of the mouth and oropharynx. May be prescribed in conjunction with systemic aureomycin therapy in cases of severe oral infections.

HOW SUPPLIED: Individually wrapped, in boxes of 10, provided with individual prescription label.

PRODUCER: Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

*Trademark.

VI-LITRON THERAPEUTIC

DESCRIPTION: Vitamin B_{12}, plus vitamins, liver and iron in capsule form. Each capsule provides:

Vitamin B_{12}	10 micrograms
Folic acid	1.0 mg.
Liver concentrate	300 mg.
Ferrous sulfate	195 mg.
Ascorbic acid (C)	50 mg.
Thiamine HCl (B_1)	2 mg.
Riboflavin (B_2)	2 mg.
Niacinamide	10 mg.
Pyridoxine HCl (B_6)	0.5 mg.
d-Calcium pantothenate	1 mg.

INDICATIONS FOR USE: In the treatment of pernicious anemia, macrocytic anemias of pellagra, sprue, pregnancy; secondary hypochromic anemias; mixed macrocytic-microcytic anemias.

DOSAGE AND ADMINISTRATION: 1 to 6 capsules daily immediately after meals, or as directed by physician.

HOW SUPPLIED: Quantities of 50, 100, 200 and 500.

PRODUCER: Casimir Funk Laboratories, Inc., affiliate of U. S. Vitamin Corp., New York, N. Y.

TETRACILLIN TABLETS

PURPOSE: Combined penicillin and sulfonamides for oral therapy of infections.

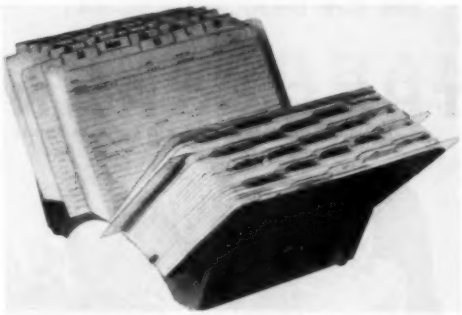
COMPOSITION: Each tablet contains:

Crystalline potassium penicillin G	100,000 units
Sulfadiazine	0.167 gm.
Sulfamerazine	0.167 gm.
Sulfamethazine	0.167 gm.

DOSAGE AND ADMINISTRATION: Adults, initial dose of 6 to 8 tablets, followed by 1 to 2 tablets every four hours until temperature is normal for 72 hours. Children, according to weight.

HOW SUPPLIED: Bottles of 10, 50 and 250.

PRODUCER: Schenley Laboratories, Lawrenceburg, Ind.



CARDINEER DESK TRAY

DESCRIPTION: Each 5" by 8" card has space for both patient's history and account (dentist's record includes tooth chart). Up to 750 records are housed in an open tray, indexed from A to Z, and entire record can be exposed for reading without removal. Cards are equipped with signalling device which indicates new billing required and which is set by the doctor at time of treatment. Further information and samples may be obtained from:

PRODUCER: Diebold, Incorporated, Canton, O.

PRE-THREADED ANACAP® SILK

DESCRIPTION: Product 991, size 000 pre-threaded surgical silk is threaded on 1¾" milliners' needles and is designed to be used once and discarded. Six threaded needles are mounted and placed in envelope for convenience in sterilizing.

PRODUCER: Davis & Geck, Brooklyn, N. Y.

DIA-DISCS

PURPOSE: Small diagnostic tablets for use in determining the antibiotic to which an infectious organism is most sensitive.

DESCRIPTION: Six different Dia-Discs are available, representing the six antibiotics in common use: penicillin, bacitracin, streptomycin, CHLOROMYCETIN,* aureomycin, and terramycin. Two potencies of each antibiotic are supplied.

Up to six tablets may be placed on a previously streaked petri plate which is then incubated overnight. The diameter of the inhibition zone surrounding each tablet gives indication of sensitivity.

HOW SUPPLIED: Boxes of 24, each tablet individually sealed in pliofilm, together with a sensitivity chart.

PRODUCER: C. S. C. Pharmaceuticals, New York, N. Y.

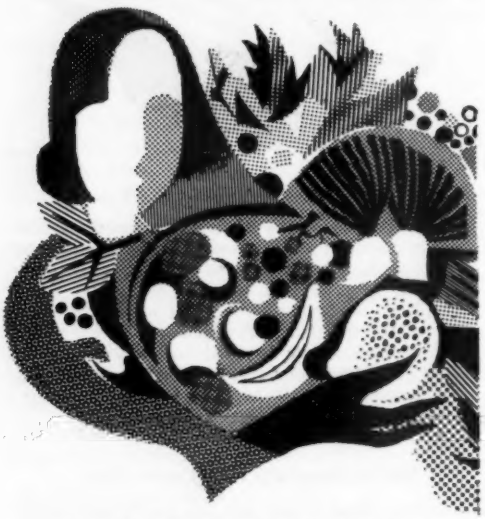
(Continued on page A-52)

Multiple Vitamin Deficiencies

". . . Deficiency diseases clinically evident are usually associated with additional tissue deficiencies of nutrients not yet clinically manifest." (Jolliffe, Tisdall & Cannon: Clinical Nutrition, New York, Hoeber, 1950, p. 633-634.)

THERAGRAN

THERAPEUTIC FORMULA VITAMIN CAPSULES SQUIBB



—supplies all of the vitamins indicated in mixed vitamin therapy in the clinically proved, truly therapeutic "practical formula"* recommended by Jolliffe.

Each Theragran Capsule gives your patient:

Vitamin A	25,000 U.S.P. units
Vitamin D	1,000 U.S.P. units
Thiamine hydrochloride	10 mg.
Riboflavin	5 mg.
Niacinamide	150 mg.
Ascorbic acid	150 mg.

Bottles of 30, 100, and 1000

* *Thiamine content raised to 10 mg.*

for true vitamin therapy . . .

specify **THERAGRAN®**

SQUIBB

FIXED-ANGLE-HEAD CENTRIFUGE

DESCRIPTION: Powerful universal motor operates from any 110 volt service outlet, AC or DC. Silent operation is assured as motor is live-rubber suspended within the cast motor housing. Semi-oilless high speed bearings insure maximum life at high speeds. Adequate ventilation prevents overheating. Motor is equipped with a vitreous enamel rheostat with "off" position and five speeds; high speed on AC approximately 4200 RPM, DC 20 per cent faster. Machined magnesium alloy head accommodates six 15 ml. tubes which are held at a fixed angle. Shipping weight is 20 lbs.

No. L-2S6: Six-place fixed-angle-head centrifuge, complete with cone cap, underguard, six metal shields and six 15 ml. glass tubes.

No. L-2S6-B: Same as above with ball bearing motor. Maximum speed on AC approximately 5000 RPM.

PRODUCER: Phillips-Drucker, St. Louis, Mo.

PICKER FOOTSTOOL

PURPOSE: For patients who experience difficulty in getting on or off x-ray tables or in and out of bed.

DESCRIPTION: Stool cannot tip, and one can stand on any corner with complete safety. Rubber feet prevent slipping and ribbed rubber top assures a firm foothold. Overall dimensions are 8½″ high, 18″ long and 13″ wide. Platform area is 10¼ by 14″. Available with or without the side rail. The side rail model has a support 39¾″ from the floor.

PRODUCER: Picker X-Ray Corporation, New York, N. Y.

SULFAMETHAZINE

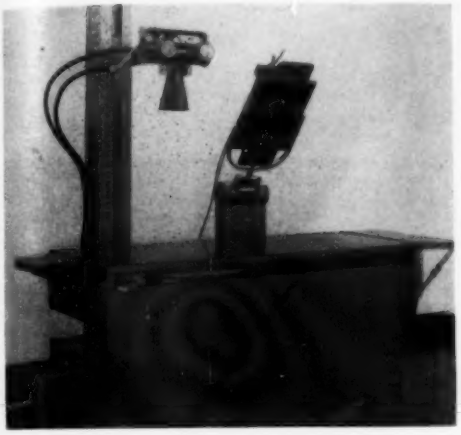
PURPOSE: Sulfonamide in tablet form.

COMPOSITION: One of the pyrimidine derivatives of sulfanilamide.

DOSAGE AND ADMINISTRATION: Dosage is adjusted to age, according to the judgment of the physician.

HOW SUPPLIED: Bottles of 100 and 1000 tablets (0.5 gm.).

PRODUCER: Sharp & Dohme, Inc., Philadelphia, Pa.



WESTEX COMBINATION X-RAY UNIT

DESCRIPTION: Available in a wide variety of one and two tube combinations with capacities from 50 to 200 MA, unit features separate floor-rail tubestand, counterbalanced tubearm with positive locks, bucky diaphragm and maneuverable fluorescent screen over entire examining area. Available in either one or two tube units with manually tilted or motor-driven table, as desired.

PRODUCER: Westinghouse X-Ray, Baltimore, Md.

DROMORAN HYDROBROMIDE

PURPOSE: Synthetic analgesic.

COMPOSITION: Chemically, Dromoran Hydrobromide is dl-3-hydroxy-N-methylmorphinan hydrobromide. Classified as a narcotic.

DESCRIPTION: Properties are similar to those of morphine, meperidine and METHADON.* On subcutaneous administration, Dromoran is more potent and longer acting than morphine. It depresses respiration to approximately the same degree as morphine but less than methadon.

INDICATIONS FOR USE: Relief of severe pain, especially intractable pain due to tumors, myocardial infarction, bursitis, biliary and renal colic, and neuritis.

DOSAGE AND ADMINISTRATION: Recommended dose is from 2.5 to 5 mg. (½ to 1 cc.).

HOW SUPPLIED: In 1 cc. ampules, 5 mg. each, 12's and 100's, and in 10 cc. multiple-dose vials, 5 mg. per cubic centimeter.

PRODUCER: Hoffmann-La Roche, Inc., Nutley, N. J.

PABLUM CEREALS

DESCRIPTION: The Pablum name has been extended to all Mead Johnson's precooked vitamin-and-mineral-enriched cereals for babies. They are Pablum Mixed Cereal (the original Pablum), Pablum Oatmeal (formerly Pabena), Pablum Barley Cereal and Pablum Rice Cereal.

PRODUCER: Mead Johnson & Co., Evansville, Ind.

(Continued on page A-54)

Multiple Vitamin Therapy

". . . Patients fare much better when [the deficiencies] are treated simultaneously. . . . Convalescence is delayed when one gives only one vitamin at a time . . ." (Spies & Butt in Duncan, G. G.: Diseases of Metabolism, ed. 2, Philadelphia, Saunders, 1947, p. 504.)

THERAGRAN

THERAPEUTIC FORMULA VITAMIN CAPSULES SQUIBB

Each Theragran Capsule gives your patient:

Vitamin A	25,000 U.S.P. units
Vitamin D	1,000 U.S.P. units
Thiamine hydrochloride	10 mg.
Riboflavin	5 mg.
Niacinamide	150 mg.
Ascorbic acid	150 mg.

Bottles of 30, 100, and 1000

When you want truly therapeutic dosages—specify **THERAGRAN®**

SQUIBB

CRYSTALLINE VITAMIN A

DESCRIPTION: Crystalline vitamin A has now been produced by synthesis on a commercial scale and is available as a dry stabilized powder with a high potency of 500,000 units per gram and as a liquid with a potency of 1,600,000 units per gram. The liquid form is practically odorless and tasteless. Stability of synthetic crystalline vitamin A is such that no substantial deterioration occurs when it is exposed to air at high temperatures for 1200 hours—the approximate equivalent of storage for three years under normal conditions.

PRODUCER: Chas. Pfizer & Co., Inc., Brooklyn, N. Y.

GYNETONE INJECTION

PURPOSE: Single dose form of estrogenic and androgenic steroids for the treatment of the menopause.

COMPOSITION: Each cubic centimeter contains 1.0 mg. estradiol benzoate U.S.P. and 20.0 mg. testosterone propionate U.S.P., in sesame oil.

DOSAGE AND ADMINISTRATION: Mild cases: 0.5 cc. two to three times weekly until symptoms are well controlled; dosage is then reduced to ascertain minimum requirement. Moderate cases: Treated in same manner, using 1.0 cc. two to three times weekly as initial dosage. Severe cases (including surgical menopause, roentgen castration and cases manifesting involutional melancholia or other psychic disturbances): 1.5 cc. two to three times weekly as initial dosage.

HOW SUPPLIED: 10 cc. multiple dose vials, boxes of 1 and 6 vials.

PRODUCER: Schering Corporation, Bloomfield, N. J.

AQUASPERSE VITAMIN A C D DROPS

PURPOSE: Aqueous solution of synthetic vitamin A, C and D.

COMPOSITION: Each 0.6 cc. contains:

Vitamin A	5000 U.S.P. units
Vitamin D	1000 U.S.P. units
Ascorbic acid	50 mg.

INDICATIONS FOR USE: For patients who do not tolerate natural sources of vitamin C and those who are allergic to oil-soluble vitamins derived from fish oil sources.

DOSAGE AND ADMINISTRATION: May be given in water, milk, fruit juices or other aqueous fluids.

HOW SUPPLIED: Bottles of 15 cc. and 30 cc. with droppers calibrated for 0.3 cc. and 0.6 cc.

PRODUCER: White Laboratories, Inc., Newark, N. J.

CYCOTIN TABLETS

PURPOSE: Appetite depressant.

COMPOSITION: Each tablet contains:

Methylcellulose	500 mg.
d-Amphetamine phosphate	1.67 mg.

INDICATIONS FOR USE: In obesity and in weight control.

CAUTIONS: Amphetamine should be administered with caution in the presence of hypertension or cardiovascular disease. In certain individuals, amphetamine may produce overstimulation, restlessness, sleeplessness and gastrointestinal disturbances.

DOSAGE AND ADMINISTRATION: 3 tablets with full glass of water one-half hour before meals; reduce to individual requirements.

HOW SUPPLIED: Bottles of 100, 500 and 1000.

PRODUCER: Reed & Carnrick, Jersey City, N. J.

VIFORT

PURPOSE: Formerly prepared solely as the aqueous polyvitamin solution for children, Vifort is now supplied also as a completely water-soluble polyvitamin preparation in capsule form.

COMPOSITION: One capsule provides prophylactic amounts of the nine vitamins.

INDICATIONS FOR USE: In pregnancy, lactation, intestinal and liver diseases where vitamins are poorly absorbed, steatorrheic diseases, obesity management, dermatoses associated with vitamin deficiencies, convalescence, geriatrics and during prolonged (vitamin depleting) drug therapy.

HOW SUPPLIED: Bottles of 30, 100 and 250 capsules.

PRODUCER: Endo Products, Inc., Richmond Hill, N. Y.

TABLETS ALCETIN

PURPOSE: Analgesic-antipyretic for relief of pain and mental depression which lowers pain threshold.

COMPOSITION: Each tablet represents:

Dextro-amphetamine sulfate	2.5 mg. (approx. 1/25 gr.)
Acetophenetidin	162.0 mg. (2½ gr.)
Acetylsalicylic acid	227.0 mg. (3½ gr.)

INDICATIONS FOR USE: Phlebitis, bursitis, headache, sinusitis, neuralgia, myalgia, neuritis, toothache, arthritis, dysmenorrhea, and for suppressing the fever associated with infections. Alcetin also tends to counteract the depressant effect of analgesic drugs upon heart and circulation.

DOSAGE AND ADMINISTRATION: 1 or 2 tablets three or four times daily as directed.

HOW SUPPLIED: Bottles of 100 and 1000.

PRODUCER: Pitman-Moore Co., Indianapolis, Ind.

New products approved for inclusion in this department but for which space is not available this month are listed below. Detailed descriptions of these drugs and instruments will be printed in subsequent issues.

Duoline X-Ray Film Illuminator (General Electric Co., X-Ray Dept.)
Glucose-6-Phosphate Dehydrogenase (Sigma Chemical Co.)
Haemo-Sol (Meinecke & Co.)
Hycidaron Tablets (Warren-Teed)
Ledercillin Soluble Penicillin Tablets (Lederle Labs)
Plaxpak Detergent Dispenser (Plax Corporation)
Pregnanediol Glucuronide and Estriol Glucuronide (Sigma Chemical Co.)
Provite B with Vitamin C (Ives-Cameron Co.)
Semhyten Capsules (S. E. Massengill)
Semvimin Perles (S. E. Massengill)
Terramycin Tablets (Chas. Pfizer & Co.)
Tris (Hydroxymethyl) Aminomethane (Sigma Chemical Co.)
Tryptar (Armour & Co.)
Workabinets (General Electric Co., X-Ray Dept.)

A GOOD ANSWER TO ESSENTIAL HYPERTENSION

TOLANATE

INOSITOL HEXANITRATE

Tolanate—inositol hexanitrate—usually leads to a gratifying response in essential hypertension. It produces a clinically significant and sustained drop in arterial tension by arteriolar dilatation, with practically complete freedom from "nitrite headache."

Tolanate With Phenobarbital, by its vasorelaxant and sedative action, unravels the psychosomatic knot of excessive irritability, anxiety and essential hypertension in the harassed businessman or the overworked executive.

Dosage: The average dose of Tolanate, each tablet containing 10 mg. of inositol hexanitrate, is one tablet three or four times daily.

The average dose of Tolanate With Phenobarbital, each tablet containing 10 mg. of inositol hexanitrate and 16 mg. (¼ gr.) of phenobarbital, is the same as for Tolanate, being limited by the degree of sedation desired.

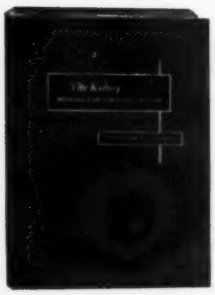
C.S.C. Pharmaceuticals

A DIVISION OF COMMERCIAL SOLVENTS CORPORATION, 17 East 42nd Street, New York 17, New York

The Medical Bookman

► THE KIDNEY; Medical and Surgical Diseases - - -

By Arthur C. Allen, M.D., Pathologist, the James Ewing Hospital; Assistant Attending Pathologist, Memorial Cancer Center, New York City; Attending Consultant in Pathology, Veterans Administration Hospital, Bronx, New York. 583 pages with 1115 illustrations. 1951, Grune & Stratton, New York. $15.00.



Although written by a pathologist, this book is directed not only toward pathologists but also to clinicians, especially urologists, and to internists and students. In it Doctor Allen fuses present knowledge of the kidney into a work that is complete in its scope and pertinent for all who are concerned with its diseases. The author draws on his vast experience in pathology as well as the extensive literature in this field.

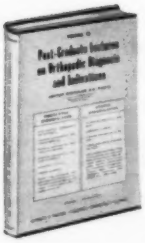
He succeeds in his aim of presenting a dynamic coverage of renal diseases, always showing relationships to their clinical facets rather than covering only their descriptive pathology. Anatomy, embryology and physiology of the kidney are presented to facilitate a comprehension of the effects of the various pathologic states. In developing each disease, pathogenesis and clinical correlations are stressed. He admits limitations of present technics and resultant gaps in our knowledge where they exist. In controversial matters such as "lower nephron nephrosis" he presents evidence for the various current opinions and withholds dogmatic interpretations.

In such conditions as lupus erythematosus, scleroderma and others with extrarenal involvement, there is brief and adequate description of the total disease process, relating the changes in the kidney to those occurring elsewhere. Generous use of excellent gross and microscopic photographs enhances these verbal descriptions. The final chapter on "Histologic Artefacts" should be of valuable aid to proper microscopic interpretations. At the end of each section is found a long list of references which are brought up-to-date and serve well as a guide to the literature on each subject.

S. S. B.

► POST-GRADUATE LECTURES ON ORTHOPEDIC DIAGNOSIS AND INDICATIONS - - -

By Arthur Steindler, M.D., F.A.C.S., Professor of Orthopedic Surgery, State University of Iowa, Iowa City. Vol. II. 208 pages with 209 illustrations. 1951, Charles C Thomas, Springfield, Illinois. $6.00.



The second of a proposed series that will eventually include four volumes has become available and is added to Dr. Steindler's already long list of distinguished publications. This book is concerned primarily with static and paralytic disabilities. In the latter, particularly in poliomyelitis, the author advises against the practice of "taking over" once the deformities have appeared. Rather he feels that the orthopedist must share the responsibilities with the pediatrician or internist from the very onset of the disease. For this reason, the etiology, pathology, clinical manifestations and differential diagnoses are presented. Such knowledge is necessary to understand the development of various residual deformities and tends to broaden the con-

(Continued on page A-58)

PUBLISHED SEPTEMBER 1951

SURGICAL CARE

A PRACTICAL PHYSIOLOGIC GUIDE

By ROBERT ELMAN, M.D., F.A.C.S.

Prof. of Clin. Surgery, Washington Univ. School of Medicine,
Director, Surgical Service, Homer G. Phillips Hosp., St. Louis

In this new text the author presents positive programs of therapy designed specifically to

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- **Reduce surgical mortality.**
- **Promote early restoration of health and functional efficiency.**

It is based on the modern concept of sound physiological and biochemical knowledge of what the human body can and cannot itself accomplish.

It acknowledges the current thinking that much recent surgical advance has been due to improved care of the patient outside the operating room and the certainty that such care has extended the field of surgery by making many more patients good operative risks even for extensive procedures.

Nutritional factors in surgery are covered in 66 pages and latest surgical uses of antibodies are discussed. Preoperative study and preparation are covered in considerable detail and some aspects of surgical diagnosis are included because they so frequently affect the postoperative course in a decisive way. Brief case reports illustrate mistakes as well as successes in therapy.

The chapters on Anesthesia and on Inhalation Therapy and Resuscitation have been contributed by Meyer Saklad, M.D., Providence, R. I.

580 Pages **75 Illustrations** **Publ. Sept. 1951** **$8.00**

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cept of their manifestations. Operative procedures are then outlined on a regional basis for immediate reference. The pathomechanics, types, prophylactic, conservative and operative treatment of paralytic scoliosis are briefly discussed.

Under static disabilities, the subject matter surveys low back pain, idiopathic scoliosis, internal derangement of the knee and deformities of the foot and ankle. A lecture on spastic paralysis is also included.

As a successor to the original work on propaedeutics and congenital deformities and disabilities, the book amplifies the more important contributions relative to paralytic and static incapacities. An excellent bibliography is tabulated and records the historical metamorphosis of various operative procedures. The author's particular faculty for this feature enriches the value of the material and allows spontaneous reference for more intensive study.

H. O'P.

► SYLLABUS OF HUMAN NEOPLASMS - - -

By R. M. Mulligan, M.D., Professor of Pathology, University of Colorado School of Medicine, Denver. 317 pages with 230 illustrations. 1951, Lea & Febiger, Philadelphia. $7.50.

Dr. Mulligan's text provides a brief survey of the pathology of human neoplasms; it is not intended as an exhaustive volume. Within its covers he presents gross and microscopic descriptions of tumors arranged by systems, along with clinical, diagnostic and therapeutic considerations. It is written in a direct, clear manner and encloses a large amount of data in a compact space. Photomicrographs of excellent quality are generously used in association with the description. A bibliography concludes each chapter.

"Syllabus of Human Neoplasms" can find a worthwhile place as a reference for clinicians; for students it can serve well as a supplementary text.

S. S. B.

► A TEXT-BOOK OF X-RAY DIAGNOSIS by British Authors in Four Volumes - - -

Ed. 2, edited by: S. Cochrane Shanks, M.D., F.R.C.P., F.F.R., Director, X-Ray Diagnostic Department, University College Hospital, London; and Peter Kerley, M.D., F.R.C.P., F.F.R., D.M.R.E., Director, X-Ray Department, Westminster Hospital; Radiologist, Royal Chest Hospital, London. Volume 1—434 pages with 439 illustrations; volume 2—702 pages with 605 illustrations. 1951, W. B. Saunders Company, Philadelphia & London. Vol. 1, $12.00; vol. 2, $15.00.

With the rapid advances in roentgenology there has been a need for complete and authoritative texts on the subject. In 1939 the first edition of the "British Authors," as the publication has popularly been called, was accepted as an outstanding text and reference book. During and immediately following World War II there were five re-printings of the original text, all of which have been eagerly sought by students and practitioners of radiology. In a medical field which has grown and continues to grow as rapidly as radiology it is necessary to revise such a text after about 10 years. The present revision meets this demand. There have been 17 contributors to the four parts of this work, of which the first and second volumes are being reviewed in this report.

The first volume concerns itself with discussions of the central nervous system, the teeth and jaws, the eyes, the accessory nasal sinuses, and the ears and temporal bones. The authors have made wide use of the recent advances in the literature, and the contributions of American and European investigators have been well documented. A section on cerebral angiography has been added to this edition. The discussion of the methods of angiography is complete and the representative films are excellently chosen. In the section on diagnosis of spinal cord lesions with myelography the author has discussed only oil myelograms; the Scandinavian method of using water-soluble contrast mediums has not been covered.

Volume 2 is concerned entirely with the cardio-

(Continued on page A-60)

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4. Described the diseases of the thyroid in relation to the newer understanding of its physiology—and has stated the clinical features and management of these diseases with real simplicity.

5. Turned over the surgical approach to the thyroid to well qualified surgeons whose contribution forms a separate section of the book. The historical chapter has also been segregated.

By THOMAS HODGE McGAVACK, B.A., M.D., F.A.C.P.

Professor of Clinical Medicine, New York Medical College; Director of the New York Medical College, Metropolitan Hospital Research Unit.

With a Section on Surgery by JAMES M. WINFIELD, B. A., M. D., F. A. C. S., Professor and Director of Surgery, New York Medical College; and WALTER L. MERSHEIMER, B. S., M. D., F. A. C. S., Associate Professor of Surgery, New York Medical College; and a Section on History by DOROTHY B. SPEAR, Ph. B., Librarian and THOMAS HODGE McGAVACK.

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vascular and respiratory systems. Peter Kerley has written both sections. In the presentation of congenital heart lesions Dr. Kerley demonstrates some of the newer innovations in the methods of roentgen diagnosis such as angiocardiography and the roentgen observation of cardiac dynamics. In the section on diagnosis of lung tumors, tomography is well discussed and illustrated.

J. F.

► BLOOD GROUPS IN MAN - - -

By R. R. Race, Ph.D. (Cantab.), M.R.C.S. (England), Director, Medical Research Council Blood Group Research Unit, Lister Institute, London, and Ruth Sanger, Ph.D. (London), B.Sc. (Sydney), Medical Research Council Blood Group Research Unit, Lister Institute, London. 290 pages, illustrated. 1951, Charles C Thomas, Springfield, Illinois. $6.50.

The need for a useful compilation of the last decade's enormous volume of literature dealing with the blood groups in man is competently fulfilled by this book.

Emphasis is given to the problems of inheritance of the blood groups as well as to the application of blood group study methods to the science of genetics. The laboratory procedures used in blood group investigation are considered in detail, particularly in regard to Rh testing.

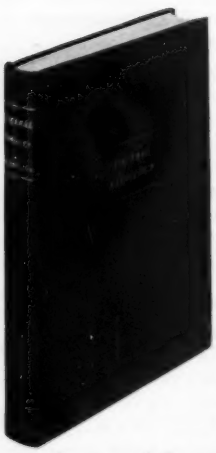
The principal blood groups (ABO, MN, P, Rh) are discussed by chapter with respect to history, inheritance, frequency and distribution, and recent work. Somewhat briefer discussions of the more recently identified blood groups are also given.

A special section of the book deals with the use of blood group principles and methods in solving problems of parentage and identity. This book contains material of interest and value to the geneticist, pathologist, physician and to members of the legal profession.

T. B. G.

► VISCERAL RADIOLOGY - - -

By Emerik Markovits, M.D., Formerly Scientific Collaborator of the Central Radiologic Institute of the General Hospital (Holzknecht-Institute), Vienna; Head of the Radiologic Department of Elizabeth Hospital of the City of Budapest; Post-graduate Lecturer at the Central Radiologic Institute of the University of Budapest; Radiologist of the Steiner Cancer Clinic, Atlanta, Georgia. 612 pages with 682 figures. 1951, The Macmillan Company, New York. $24.00.



As a complimentary volume to the previously published "Bone and Joint Radiology," the present text makes great use of the outline form of presentation and gives an excellent description of the anatomy and physiology of the organ just prior to the discussion of its pathology. The book is divided into six sections: (1) chest and respiratory system, (2) circulatory system, (3) digestive system, (4) abdomen and abdominal organs, (5) genitourinary system and (6) the central nervous system. Because of the extent of the material covered, the detail of each particular system is necessarily condensed, and this condensation has been expertly done so as to make the major significant factors stand out to the student.

In discussion of the pneumoconioses, the descriptions of the occupational hazards and of degrees of exposure to dust have been adequately expressed, and the nature of the pathology has been described so that the student can better understand the variability of the x-ray shadows which may appear in this disease. The material on the abdomen and the abdominal contents is inadequate inasmuch as the number of conditions of the acute abdomen which can be diagnosed radiographically are not completely emphasized. A very brief discussion of the lesions of the central nervous system is presented in outline form.

The charts on differential diagnosis are important to the beginning student as they help him analyze a film and direct his attention to important signs which he may otherwise overlook. The

(Continued on page A-62)

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By Bernardo A. Houssay, M.D., Juan T. Lewis, M.D., Oscar Orias, M.D., Eduardo Braun-Menendez, M.D., Enrique Hug, M.D., Virgilio G. Foglia, M.D., and Luis F. Leloir, M.D. 1951. 1118 pages, 7¼ x 9⅞, 499 illustrations. $14.00

"This textbook reveals Dr. Houssay and his associates as first-class teachers, by accuracy in facts, clarity of style, excellence of illustrations, and scientific objectivity in judgments and conclusions. Medical students, both graduate and undergraduate, will be aided, guided, and challenged by the references on nearly every page, and at the end of each of the 89 chapters . . ."

A. J. Carlson, University of Chicago in SCIENCE, *June 15, 1951*

". . . A well-balanced presentation of the various parts of human physiology, without undue overemphasis of those areas of physiological research in which the writers are particularly interested. The book will be of great value to beginning medical students who find other standard textbooks too difficult . . . Printing and binding are excellent."

J.A.M.A., *July 7, 1951*

Other books of interest to the profession

PEDIATRIC ALLERGY

By Robert Chobot, M.D., Assistant Clinical Professor of Pediatrics, New York University Post-Graduate Medical School; Director, Pediatric Allergy Clinic, University Hospital. 1951. 284 pages, 5½ x 8. $4.50

YELLOW FEVER

Edited by George K. Strode, M.D., Director, International Health Division, The Rockefeller Foundation; with contributions by eight members of the Foundation. 1951. 711 pages, 7¼ x 9⅞, illustrated. $9.50

HEALTH OBSERVATION OF SCHOOL CHILDREN

By George M. Wheatley, M.D., Third Vice-President, Health and Welfare, Metropolitan Life Insurance Company; and Grace T. Hallock. 1951. 491 pages, 6 x 9, illustrated. $4.75

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text includes a concise description of angiocardiography and cardiac catheterization, which are recent innovations. The author makes excellent use of line and shadow sketches to illustrate pathology, especially in lesions of the stomach and gastrointestinal tract.

Correlation of basic anatomic, physiologic and pathologic data and x-ray findings is an excellent method of presentation for the beginning student in radiology and for medical students. The text serves its best purpose in this field. It is not of sufficient detail to be used as a reference book by the practitioner of radiology, but it may prove of occasional value by providing an excellent didactic method of presentation of x-ray material to his students and his colleagues.

J. F.

► A TEXTBOOK OF MEDICINE - - -

Edited by Russell L. Cecil, M.D., Sc.D., Professor of Clinical Medicine, Emeritus, Cornell University, New York, and Robert F. Loeb, M.D., Bard Professor of Medicine, Columbia University, New York. Associate Editors: Alexander B. Gutman, M.D., Professor of Medicine, Columbia University, New York; Walsh McDermott, M.D., Associate Professor of Medicine, Cornell University, New York; Harold G. Wolff, M.D., Associate Professor of Medicine (Neur.), Cornell University, New York. Ed. 8. 1,627 pages with 204 figures and 40 tables. 1951, W. B. Saunders Company, Philadelphia & London. $12.00.

A description of a book of this kind is feasible and admissible; a review is impossible and would be presumptuous. The table of contents occupies 31 pages, the index requires 77 pages of triple column type and the textual matter extends through 1,550 double column pages.

One hundred and sixty-eight authors have collaborated in presenting an acceptable introduction to internal medicine. The subjects are treated in accurate, synoptic manner, with some elaboration of detail for major diseases and conditions. The information is for the most part up-to-date, although some recent therapeutic suggestions are apparently not mentioned. But 20 subjects not found in the seventh edition are discussed, such as Q fever, collagen diseases, vitamin B_{12} deficiency and phenylpyruvica oligophrenia.

The substance is arranged in the pattern traditional for medical texts and is laudably conservative, suitable for students and general practitioners.

J. B. C.

► HEMODYNAMICS IN FAILURE OF THE CIRCULATION - - -

By W. B. Youmans, M.D., Ph.D., Professor of Physiology, University of Oregon Medical School, and A. R. Huckins, M.S., M.D., Research Assistant, Department of Physiology, University of Oregon Medical School, Portland. 71 pages. 1951, Charles C Thomas, Springfield, Illinois. $2.75.

A monograph in the American Lecture Series, this book is presented in four major divisons dealing with: (1) basic physiologic principles such as the relationship between ventricular filling and strength of ventricular contractions, venous pressure and reflex effects upon rate and strength of ventricular contractions, and the relationship between cardiac output, renal blood flow, and blood volume; (2) failure of venous return; (3) failure of the heart; and (4) chronic venous congestion without failure.

The authors do not present any original research work of their own, but have collected the literature containing pertinent measurements in patients with failure of the circulation; they quote 200 references. They have taken the available data and presented controversial points with their own interpretations. Particular emphasis is placed on venous pressure and various aspects of heart failure, and there is discussion of the probable mechanisms by means of which the left ventricular failure may lead to an elevation of both pulmonary and systemic venous pressure.

The authors state that the article was written primarily for three classes of readers: (1) those considering the subject of failure for the first time; (2) those who have had no opportunity to do systematic reading on the subject during recent years, and (3) those who wish to review the subject in the light of basic physiologic facts. Current controversial phases of the problem are clearly presented together with possible explanations.

Y. S.

(Continued on page A-64)

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Interstate Postgraduate Medical Association, St. Louis, October 22-25, 1951

SOFFER—DISEASES of the ENDOCRINE GLANDS
By Louis J. Soffer, M.D., Mount Sinai Hospital, New York. *New. 1142 pages. 88 illus. and 3 plates in color.* $15.00

RITVO—CHEST X-RAY DIAGNOSIS
By Max Ritvo, M.D., Harvard Medical School. *New. 358 pages, 7" x 10". 615 illus. on 418 figs. and 1 plate in color.* $15.00

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By Samuel M. Peck, M.D., Columbia University, and George Klein, M.D., New York Medical College. *New. 383 pages. 4 illustrations.* $6.50

ELLER and ELLER—TUMORS of the SKIN
By Joseph J. Eller, M.D., New York City Hospital; and William D. Eller, M.D., New York City Hospital, N. Y. *New (2nd) Edition.* *Just Ready*

HOLMES and SCHULZ—THERAPEUTIC RADIOLOGY
By George W. Holmes, M.D., Waldo County General Hospital, Belfast, Maine; and Milford D. Schulz, M.D., Harvard Medical School. *347 pages. 121 illus., 10 in color.* $7.50

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By 33 Contributors. Edited By Roscoe L. Pullen, M.D., F.A.C.P., Director, Division of Graduate Medicine; and Vice-Dean, School of Medicine, Tulane University, New Orleans, La. *1035 pages, 6½" x 10". 253 illus. and 35 in color.* $20.00

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With 65 Contributors. Edited by Michael G. Wohl, M.D., Temple University School of Medicine. *New (5th) Edition.* *Just Ready*

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By Emanuel Goldberger, M.D., Montefiore Hospital, New York. *New Book. 651 pages. 229 illus. on 90 figures.* $10.00

TOWN—OPHTHALMOLOGY
By Arno E. Town, M.D., Jefferson Medical College, Philadelphia. *New. 511 pages. 208 illustrations and 4 plates in color.* $10.00

MULLIGAN—SYLLABUS of HUMAN NEOPLASMS
By R. M. Mulligan, M.D., University of Colorado School of Medicine. *New Book. 317 pages, 7" x 10". 230 illus.* $7.50

EPSTEIN—REGIONAL DERMATOLOGIC DIAGNOSIS
By Ervin Epstein, M.D., Stanford University Medical School, California. *328 pages. 148 illus.* $6.00

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► DISEASES OF THE ENDOCRINE GLANDS . . .

By Louis J. Soffer, M.D., F.A.C.P., Associate Attending Physician and Head of the Endocrine Research Laboratory and Clinic, The Mount Sinai Hospital, New York City; Assistant Clinical Professor of Medicine, Columbia University. 1142 pages with 88 illustrations and 3 plates in color. 1951, Lea & Febiger, Philadelphia. $15.00.

An outstanding textbook of endocrinology by a foremost authority in the field, this book will prove valuable to the student, teacher, general practitioner and specialist alike. It is well illustrated and contains numerous case reports illustrating the diseases discussed.

The text is divided according to gland, and heading each chapter is a discourse on the basic aspects, embryology, anatomy and histology. Next the physiology, both normal and pathologic, of the endocrine gland under discussion is presented, permitting full understanding of the complete clinical treatise which follows.

The method of presentation facilitates most efficient use of the book. For example, physicians well versed in endocrinology will appreciate the careful and unbiased review of apposite literature characteristic of all sections but especially those dealing with physiology and therapy. Yet neophytes in the field of endocrinology will find excellent guidance in this sometimes complex branch of medicine.

Dr. Soffer's extensive clinical experience is reflected by the excellence of the sections on diagnosis and management. Practitioners will enjoy the close attention given to details of therapy.

The final chapter of the book, which exemplifies the consideration given to the pragmatic, presents 33 of the most commonly required laboratory tests for endocrine function. Preparation of reagents used, step by step performance of each test, and normal values are given. Both the chemical and flame photometer methods of determining electrolytes in blood and urine are described. Also included are tests for serum iodine, 17-ketosteroids, urinary corticoids and gonadotropins, ACTH eosinophil response, glucose and insulin tolerance, pregnancy and many others.

T. B. G.

► PRINCIPLES AND PRACTICE OF OBSTETRICS . . .

By J. P. Greenhill, M.D. (originally by Joseph B. DeLee, M.D.), Attending Obstetrician and Gynecologist, The Michael Reese Hospital; Obstetrician and Gynecologist, Associate Staff, The Chicago Lying-In Hospital; Attending Gynecologist, Cook County Hospital; Professor of Gynecology, Cook County Graduate School of Medicine. Ed. 10. 1020 pages with 1140 illustrations on 864 figures, 194 in color. Philadelphia, W. B. Saunders Company, 1951. $12.00.

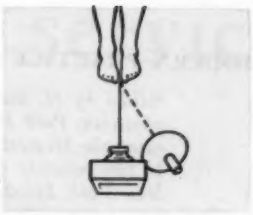
In this 1951 revision of a classical textbook of obstetrics, J. P. Greenhill now assumes full responsibility for the text. This revision has been rewritten and there has been some change in arrangement. A chapter of particular interest to this reviewer is that by Dr. Helene Deutsch on the "Psychology of Pregnancy, Labor and the Puerperium" which is based on her book, "The Psychology of Women." Other new material which has been added includes data on the physiology of the uterus, the simplified treatment of placenta previa and abruptio placentae, the importance of acute infectious diseases early in pregnancy as a cause of fetal deformities, and much new data on the use of the various antibiotics in the treatment of puerperal infection.

Greenhill, Titus, McCormick and Eastman—all of whom are authors of textbooks of obstetrics—have agreed on their definitions of certain terms, classifications and procedures about which there has been considerable controversy in the past. This material includes simple classifications of the toxemias of pregnancy, types of breech presentations, types of placenta previa and also their definition of engagement and station of the presenting part. They agree further that external pelvic measurements of the inlet are of no value, an opinion which many obstetricians have shared for many years.

The book is well arranged and the print is easily readable. New illustrations which have been added are good. This revision ranks high in this reviewer's opinion as an excellent text covering all aspects of obstetrics for anyone who is interested in the field.

M. A.

(Continued on page A-66)



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► MODERN PRACTICE IN INFECTIOUS FEVERS - - -

Edited by H. Stanley Banks, M.A., M.D. (Glas.), F.R.C.P., D.P.H., senior physician, Park Hospital, Hither Green, London; Lecturer in Infectious Diseases, the Medical College, St. Bartholomew's Hospital, University of London. In two volumes. 989 pages with 211 illustrations. 1951, Paul B. Hoeber, Inc., New York. $20.00.

Dr. Banks and an illustrious group of co-authors have written a book which adequately fulfills the need for a comprehensive text on infectious diseases. Parasitic diseases, tuberculosis and venereal diseases have been excluded. The authors, for the most part, are English but the list includes some from the United States and elsewhere.

Volume I is devoted to ecology, epidemiology, laboratory diagnostic aids, immunization and the bacterial infectious diseases. Volume II includes discussions of the viral diseases and a somewhat brief survey of infectious diseases due to rickettsiae, spirochetes, protozoa, fungi and unknown agents.

As in any text written by many authors, there is some variation in style but, for the most part, this book is a pleasure to read. The chapters are well organized and usually very complete. Each ends with a good bibliography and there is an adequate index.

W. H. H.

Books received will be acknowledged in this department each month. As space permits, books of principal interest to our readers will be reviewed more extensively.

Proceedings of the First Research Conference on Psychosurgery, New York, New York, November 17 and 18, 1949; Criteria for the Selection of Psychotic Patients for Psychosurgery. Chairman, Fred A. Mettler, M.D., Ph.D. Editor, Newton Bigelow, M.D. Public Health Service Publication No. 16. Federal Security Agency, National Institutes of Health. Copies may be purchased from Superintendent of Documents, Government Printing Office, Washington 25, D.C. $1.00.

Chronology of Ophthalmic Development; An Outline Summary of the Anatomical and Functional Development of the Visual Mechanism Before and After Birth. By Arthur H. Keeney, M.D., Wills Eye Hospital, Philadelphia. 32 pages with 3 charts. 1951, Charles C Thomas, Springfield, Illinois. $2.00.

Diabetes Control. By Edward L. Bortz, M.D., Chief of Medical Service B, The Lankenau Hospital; Associate Professor of Medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia. 264 pages, illustrated. 1951, Lea & Febiger, Philadelphia. $3.50.

Causalgia. By Frank H. Mayfield, M.D., Assistant Professor of Clinical Surgery, College of Medicine, University of Cincinnati; Attending Neurological Surgeon, Bethesda Hospital, Christ Hospital, Deaconess Hospital, Good Samaritan Hospital, St. Francis Hospital and Jewish Hospital, Cincinnati, Ohio. 65 pages, illustrated. 1951, Charles C Thomas, Springfield, Illinois. $2.25.

The Medical Works of Hippocrates. A new translation from the original Greek made especially for English readers by the collaboration of John Chadwick, M.A. (Cantab.), sometime Scholar of Corpus Christi College, Cambridge, and W. N. Mann, M.D. (Lond.), F.R.C.P., Assistant Physician to Guy's Hospital, London, England. 301 pages. 1951, Charles C Thomas, Springfield, Illinois. $5.50.

Pharmacology of the Failing Human Heart. By John McMichael, M.D., F.R.C.P., Professor of Medicine, University of London at the Post-Graduate Medical School of London. 63 pages, illustrated. 1951, Charles C Thomas, Springfield, Illinois. $2.00.

Bacterial Toxins. By W. E. van Heyningen, M.A., M.Sc., Ph.D., Senior Research Officer, Sir William Dunn School of Pathology, University of Oxford, England. 133 pages. 1951, Charles C Thomas, Springfield, Illinois. $3.50.

Clinical Urography; An Atlas and Textbook of Roentgenologic Diagnosis. By William F. Braasch, M.D., Emeritus Consultant in Urology, Mayo Clinic; and John L. Emmett, M.D., Consultant in Urology, Mayo Clinic, Rochester, Minnesota. 736 pages with 1,361 figures. 1951, W. B. Saunders Company, Philadelphia & London. $25.00.

Clinical Hematology. By Maxwell M. Wintrobe, M.D., Ph.D., Professor and Head of the Department of Medicine and Director, Laboratory for the Study of Hereditary and Metabolic Disorders, University of Utah, College of Medicine, Salt Lake City. Ed. 3, thoroughly revised. 1,048 pages with 220 illustrations and 17 plates, 13 in color. 1951, Lea & Febiger, Philadelphia. $12.50.

Manual Therapy. By James B. Mennell, M.A., M.D., B.C. (Cantab), Consulting Physician in Physical Medicine, St. Thomas' Hospital; Vice-President and Hon. Fellow, Chartered Society of Physiotherapy, London, England. 64 pages, illustrated. 1951, Charles C Thomas, Springfield, Illinois. $2.25.

Children's Radiographic Technic. By Forrest E. Shurtleff, R.T., The Children's Medical Center, Boston, Massachusetts. 80 pages with 32 illustrations and 41 tables. 1951, Lea & Febiger, Philadelphia. $3.75.

Prothrombin Deficiency. By Rosemary Biggs, M.D., Department of Pathology, Radcliffe Infirmary, Oxford. 83 pages. 1951, Charles C Thomas, Springfield, Illinois. $2.50.

Surgery of the Stomach and Duodenum; A Handbook of Operative Surgery. By Claude E. Welch, M.D., Associate Visiting Surgeon, Massachusetts General Hospital; Clinical Associate in Surgery, Harvard Medical School, Boston. Illustrated by Muriel McLatchie Miller. 349 pages with 79 plates. 1951, Year Book Publishers, Inc., Chicago. $8.50.

Pioneer Doctor. By Lewis J. Moorman, M.D. 252 pages. 1951, University of Oklahoma Press, Norman, Oklahoma. $3.75.

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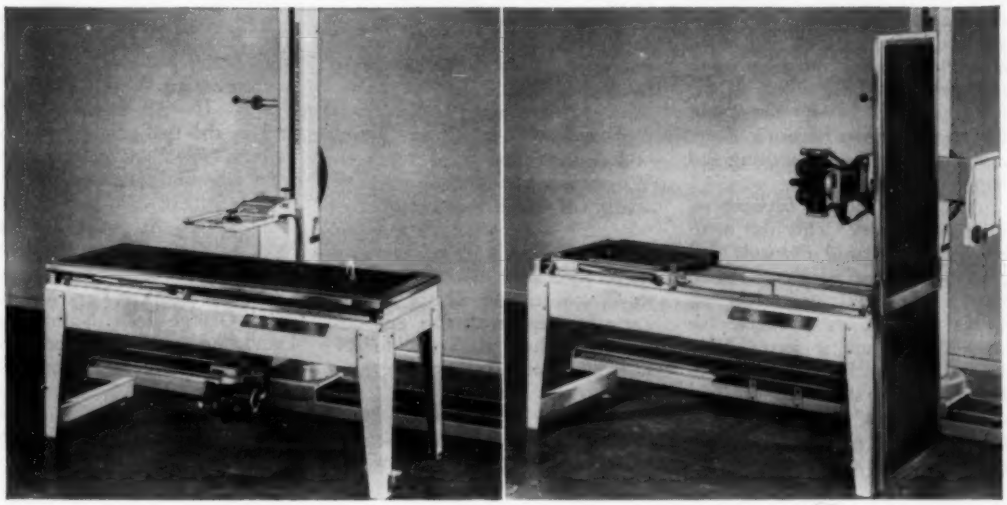


DR. Pepys' Pages

Personal Diary
and Observations on
Medical Life
by MORRIS FISHBEIN, M.D.

Aug. 1—To play at golf which I do find most relaxing and enjoyable, especially after the game is done and all the annoyance of looking up and overshooting and missing putts is forgotten.

Aug. 2—Come Eunice Stevens of Blakiston to luncheon at the Quadrangle Club and there saw Fred Hodges, the roentgenologist, and Dallas Phemister, and chatted with the physiologist Gerard about a work on his subject.

Aug. 4—To Ravisloe and acted as auctioneer for the Calcutta where Milton Reynolds of the ballpoint pens led the buying.

Aug. 5—More golf and after that mathematics with conspicuous failure.

Aug. 6—All this day at the desk with much work, preparing for travel, which means organizing the system of work and writing in advance to meet all the deadlines.

Aug. 7—With the Finnegans to the Washington Park race track and Mistress Pepys won the daily double amounting to $113.30 and did well with individual bets also.

Aug. 8—To the airport to greet Connie Traeger from New York with Miss Lawry of the Multiple Sclerosis Foundation, and then to a luncheon with the Chicago philanthropists who support research in this field—in particular, Hefter, Abeles and Abrams. In the evening with them to the Tavern Club and here came the neurologists Bucy, Pollock, Slight, and the dean Coggeshall and the ladies and we had good food and much conversation about the art of cooking and such like, sitting in the open air with the sky above and the great buildings towering about, and altogether a most exciting and happy evening.

Aug. 10—The day between replete with work. This day with the Finnegans and Francois and Antoinette Pope again to Washington Park and again Mistress Pepys won the daily double for some $36.00 and it seems Lady Luck smiles on her. Thereafter to Phil Schmidt's for the fish and chicken which draw thousands from faraway places. And Francois Pope told how he had given his television program on Creative Cookery telling of the way to prepare spareribs and that afternoon by 3:00 p.m. not a butcher in Chicago had any spareribs remaining. That's what is meant by the standardization of living through television.

Aug. 11—At night with Justin and Ann to dine at Algauer's on Wiener schnitzel and to see their apartment which is to the queen's taste, for that's what Ann seems to be. Earlier to a tea at the Bachmeyer's for he retires soon to move to Cincinnati and all the faculty came to speak with this gracious couple of their plans and to say how all hoped they would come often to visit again.

Aug. 14—More golf and reading, in particular "The Lost Library," by Walter Mehring, which tells of the books his father collected in their home in Berlin, and how the Hitler savages drove him out and how the books came along to him in Vienna. As he unpacks the books he comments on their significance in our culture:

> ". . . the fact is, or has been up to now at any rate, that all the colossal histories of the generals and the courage of their armies, all the fervor of the revolutionaries who free the people from their yoke—at tout le reste—would not last any longer than a soap bubble if these things were not condensed into literature and preserved in libraries. The men who make history owe their conquest of posterity solely to literature."
>
> "Unfortunately no movement, no matter what its direction, can go on indefinitely without wearing out."

To the Crerar Library to commune for some hours with the medical periodicals and in the evening with Larry Joselit, Sidney Portis, I. Rosenthal and E. Schuhmann at bridge, and came away with all the spoils of a series of very good hands.

Aug. 15—From London came Charles Tucker, and with him and his son Jolyon and Josh Spiegel and Friedell to play at golf, and Charles did the whole course with irons, 2 and 5 and 7 and the putter, and came out as well as those carrying an entire complement of clubs. In the evening for a farewell dinner with the family to the Porterhouse Room of the Hotel Sherman, where food is of the best, and found the waiters and the magicians were in some instances medical students earning their way and rejoiced that this spirit is not yet dead in the study of the dear art.

Aug. 16—All day at my stint and in the twilight on the CENTURY to New York meeting on the train Edmund Jacobson and my brother Albert.

Aug. 17—At work in New York arranging passage and conferring with many businesses, and to dine at night at "21" and saw there George Jean Nathan and Dr. Lempert, and gossiped with Ernie Fisher and his sweet lady of Indianapolis and the days when we were neighbors on Meridian Street. Before going to bed read

(Continued on page A-78)

OLD PEPYS' MISCELLANY

SCHOOLBOY HOWLERS

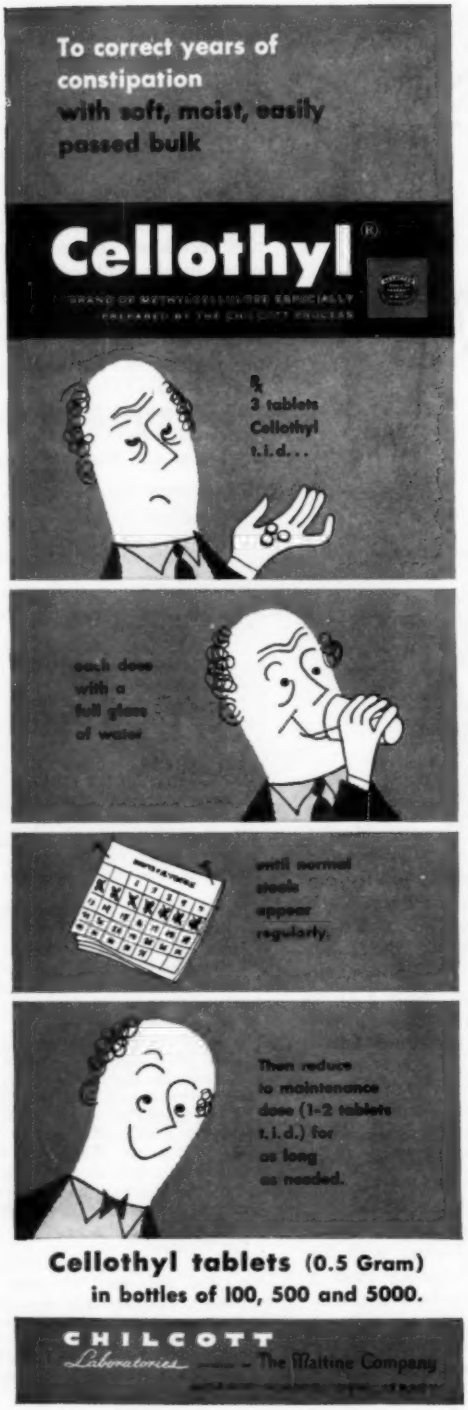
Cloaca Maxima was the first empress of Rome.

Henry the Eighth of England had a large abbess on his knee, which made walking difficult.

THE SEVEN AGES OF MAN AND COW

1. Mother's milk.
2. Cereal and cow's milk.
3. Milk, eggs and spinach.
4. Malted milk and hot dogs.
5. Vichysoisse or milk-potato soup, Long Island duckling, creamed potatoes, creamed broccoli, ice cream.
6. Soft boiled eggs, toast and milk.
7. Crackers and milk.

* * *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each dose with a full glass of water
until normal stools appear regularly.
Then reduce to maintenance dose (1-2 tablets t.i.d.) for as long as needed.
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IMPROVING RECTAL COMPETENCE IN DYSCHEZIA

When diminished tonus and contractibility have rendered the rectum incompetent, "there can be no doubt" that Cellothyl is "of great value."[1] Ease and frequency of bowel movements can be increased regardless of duration of dyschezia[1] — provided, of course, that patients who have suffered for years do not expect overnight correction. Steady improvement in the expulsive competence of the rectum will be noted with Cellothyl as the presence of adequate soft bulk and its gentle mechanical stimulation act to —

1. initiate the call to stool
2. encourage prompt, complete evacuation
3. provide soft, moist, easily passed stools
4. eliminate the need for straining
5. minimize pain or trauma to local lesions.

The stomach and small intestine, usually not involved in dyschezia, are unaffected by Cellothyl, which remains in a fluid state until it reaches the colon. Here it thickens to a smooth gel to provide bulk where bulk is needed. Normal, easily passed stools usually begin in 3 to 4 days. (Patients conditioned to purgation may be permitted a mild laxative, together with Cellothyl for several days, then Cellothyl continued alone.) As ease and frequency of defecation increase, dosage should be decreased to the minimum required for comfortable function.

1. Newey, J. A., and Goetzl, F. R.: Permanente Med. Bull. 7:67 (July) 1949.

"World Digest," which has a sketch of Sir Lionel Whitby, now regius professor of physic at Cambridge. He was a great footballer, lost a leg in the battle of the Somme, went back to Cambridge after the war to graduate in medicine, did research at Middlesex and, at age 32, was called in consultation on the care of the King. Four things, he said after World War II, have most greatly advanced modern medicine in war: forward-area surgery with modern equipment; blood transfusion; antibiotic drugs and evacuation of the wounded by air. And read a note about a cannibal who was chewing up the pictures of people from *Life:* "Tell me," said another cannibal, "is that dehydrated stuff any good?"

Aug. 18—Read a novel called "Blow Hot, Blow Cold," by Gerald Butler, which turned out to be hot and cold and heavily diluted Hemingway. In the afternoon played mathematical games with Chuck Rhein, Charles Wilinsky and Mark Soroko. Fun and profit! At night to dine with the Lasdons in Scarsdale and along came some local experts: fun and no profit.

Aug. 19—Conferring with Charles Wilinsky concerning hospital and doctor problems; then to dine at Lindy's and met Chuck Rhein and his lady, and then to see Milton Berle with Dagmar at the Roxy. What a combination! "That recent marriage of Rockefeller," commented Berle, "That's a baby marriage. He gave her blocks to play with—46th Street, 47th Street, 48th Street!" And then, to earn even more applause, Dagmar just bowed, and bowed, and bowed. In New York they call a "dagmartini" one with two olives!

Aug. 20—At the Waldorf with more and more meetings: breakfast with Wilbur Craft of Merck, and lunch with Herb West of BBD&O. Then come a multitude to dinner in the Sert Room for Basil O'Connor which Mistress Pepys arranged with the aid of Phillipe . . . George Gallup, Bernard Gimbel, Elmer Bobst, Jim

FROM THE DOCTOR'S PRACTICE

Dr. Frank was examining her for employment. She had moderate acne on her back.

"Are the pimples worse around your period?" he asked.

"Oh no!" she said. "They are just on my back."

* * *

Kerrigan, Howard Fonda, Herb Mayes, Milton Lasdon, Doug Black, Milton Runyon, Murray Breese, and all the ladies, and many more with much joyous revelry. Then Mistress Pepys made a talk about friendship and Basil replied and some of the ladies wept which made it even more enjoyable. Thereafter with Charles McCabe and his dear lady and Margaret Eagan and some others to the roof of the St. Regis and so the evening ended on a high—very high for some—note.

Aug. 21—Conferences with Doubleday and *Good Housekeeping,* and talked with DeWitt Wallace of *Reader's Digest.* In the evening come Willard Greenwald and Nellie, and Jake Geiger with his lady from San Francisco after a stay in India where he found conditions very much tsk tsk tsk.

Aug. 22—Early indeed to the QUEEN MARY where come also the Van Ripers and the Runyons and the Sorokos and others to say fond farewells, and at noon amidst a profusion of flowers and fruits and books and magazines and gallons of champagne past the Statue of Liberty and out to sea. In the afternoon Ethel Barrymore and Maurice Evans in a gruesome thriller entitled "Kind Lady."

Aug 23—The shipboard routine: breakfast in bed; work till noon; lunch; walk on deck; read; a movie; cocktail party; dinner; Bingo or horseraces; dancing; sleep. Day after day; night after night. Isn't it terrible! At our table: Basil O'Connor and Betty Ann O'Connor Culver, marvelously recovered from polio, and Dorothy Ducas and Margaret Eagan.

The Literary Bill of Fare:

Woman's Home Companion—Turnley Walker's "Journey Together." Story of a battle against polio told with literary finesse.

Charlotte Armstrong—"Black-eyed Stranger." A really tough detective story.

Calvin Tomkins—"Intermission." Novel about himself and his brother and his family by a Princeton neophyte. B- in English 3.

Charles F. Coe—"Pressure." An old *Saturday Evening Post* writer proves he can still do it with a couple of paragraphs the *Post* would never print!

Senator Estes Kefauver—"The Trials." Television come to life!

Noel—"I Killed Stalin." Something that may never happen but it might, and out of it a thriller that is a sleep-killer.

Richard Starnes—"The Other Body in Grant's Tomb." Tricky detective story.

Town and Country—Wonderful stories of Indiana and the Hoosiers.

Holiday—Richmond, Va., and Broadway.

The Movie Fare:

Show Boat—Better than ever with Ol' Man River sung by William Warfield better than Robeson.

The Frog Men—Thrills with the underwater demolition teams. Marvelous movie with a men-only cast.

The Man in the White Suit—British picture about a chemist in the textile industry who develops an indestructible waterproof non-soiling fabric. Best of the lot.

The Weather:

Two days and nights in which the ship rolled and tossed, 50 people were injured and Mistress Pepys came through by the grace of God and DRAMAMINE.

The People:

Dr. and Mrs. Johnston of Long Beach, California, who won in Bingo over and over.

(Continued on page A-80)

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*Downing, J. G. et al.: J.A.M.A. 133:299 1947. Shipley, E. R. et al.: Surg. Gynec. & Obst. 84:366 1947. Wawro, N. W.: Connecticut M. J. 12:17 1948. McCollough, N. C.: Indust. Med. 16:128 1947. Long, P. H.: A-B-C's of Sulfonamide and Antibiotic Therapy, Philadelphia, W. B. Saunders, 1948, p. 152. Meyer, J. H.: J. Internat. Coll. Surg. 13:748 1950.

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Dr. Rushing of Longview, Texas, who was one of my students at Rush.

Dr. and Mrs. David P. C. Lloyd of Rockefeller Institute, who are fun at cocktails and everywhere.

Dr. Maguire is the ship's doctor and when the ship rolled he was surely busy. One old lady fell on her back out of her chair. Said Mistress Pepys: "She showed everything she had." Commented old Pepys: "And a couple of things she didn't have."

Aug. 27—At Southampton and on the train met the Rheinharts of Wilmington where he is with du Pont, and he wore a shirt made of *dacron,* which is better than *nylon,* and she in ecstasy over seeing London. To the train came Miss Frazer of the *Evening Standard* to interview old Pepys on his interests and hobbies. Then at midnight in Claridge's in London.

Aug. 28—Reading "Defender's Triumph," by Edgar Lustgarten, which tells of some famous trials with some marvelous medical evidence introduced. At night to see Robert Morley in "The Little Hut," a naughty comedy with innumerable double entendres, and afterward to the Bagatelle where was Sonny Tufts at a table and a variety of people from all over the world, and the best Venezuelan rhumba orchestra and a singer reminiscent of Hildegarde named Celia Lipton. At Basil O'Connor's cocktail party meeting Sir Godfrey Vick and the Luques and Snyders and Millers.

Aug. 29—All the morning with Hugh Clegg and the library of the British Medical Association and all the American medical magazines on the shelves were of April and May with a few dated June.

Aug. 30—To the Cunard and the bank and to visit Foyle's and other book shops. At noon come Winifred Nerney of London Doubleday to talk of the literary scene. In the afternoon at my scrivening and at night to see a new Terence Ratigan farce—new to me, that is—called "Who Is Sylvia," and she seems to be the various ladies at various times in the hearts of men, or just another name for Helen.

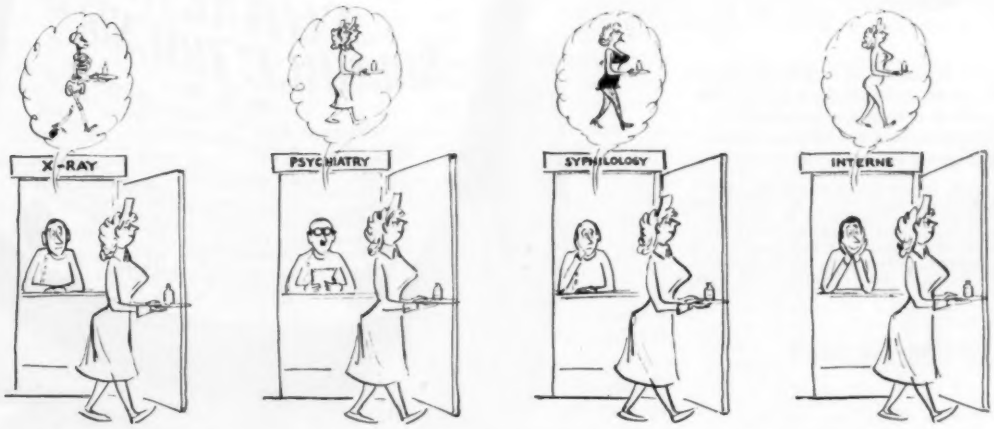
And this day came two telephone calls from English general practitioners who had seen the press notices of old Pepys' arrival and who wanted to know whether and how they might practice in America. The National Health Act would seem to be a sinking ship. The newspapers tell of a tremendous increase in cases of food poisoning because people save all the scraps of food overnight without suitable refrigeration.

FROM THE NURSES' EXAMS

An abortion is the expulsion of the contents of the uterus before the period of liability.

Intussusception is the mixing of the cells of the male and female.

A volvulus is something that happens to a vulva.



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